COUNTWAY LIBRARY
HC 4Z97 +

TUFTS COLLEGE MEDICAL & DENTAL SCHOOL
DEPT. OF ANATOMY

BOSTON
MEDICAL LIBRARY
8 THE FENWAY

Digitized by the Internet Archive
in 2025

https://archive.org/details/clinicalphysiolo0000robe

CLINICAL PHYSIOLOGY

CLINICAL PHYSIOLOGY

(A SYMPTOM ANALYSIS)

IN RELATION TO MODERN DIAGNOSIS AND TREATMENT

A TEXT FOR PRACTITIONERS AND SENIOR STUDENTS OF MEDICINE

BY

ROBERT JOHN STEWART McDOWALL

D.Sc., M.B., F.R.C.P. (Edin.)

PROFESSOR OF PHYSIOLOGY, KING'S COLLEGE, UNIVERSITY OF LONDON

WITH AN INTRODUCTION BY

W. D. HALLIBURTON

LL.D., F.R.C.P., F.R.S.,

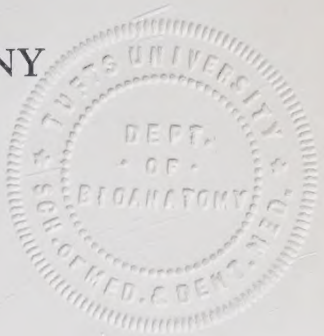
EMERITUS PROFESSOR OF PHYSIOLOGY, KING'S COLLEGE,

UNIVERSITY OF LONDON

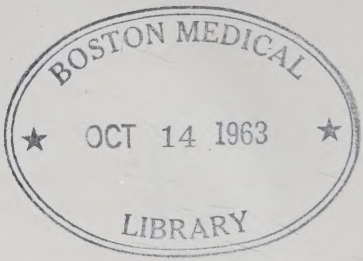
NEW YORK

D. APPLETON AND COMPANY

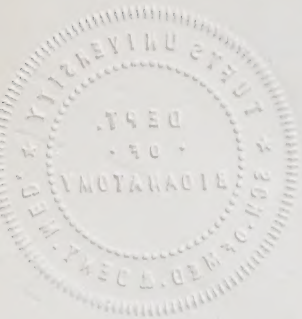
1927



COPYRIGHT, 1927, BY
D. APPLETON AND COMPANY



7 A 64



PRINTED IN THE UNITED STATES OF AMERICA

PREFACE

Some years ago it was my fortune to take an active part in the teaching of clinical medicine and, during that period, it was possible to study in some detail how far the average medical student was able to adapt his knowledge of the science of Physiology to his practical requirements. It was fully realized that the study of Physiology in its more scientific aspects was in every way desirable, but it was clearly seen that for the adequate appreciation of the signs and symptoms of disease more was necessary than is normally taught by the physiologist or clinician. It is, for example, extremely difficult—indeed almost impossible from a study of ordinary text-book Physiology—for him to see why a cardinal symptom of cardiac disease should be breathlessness.

This volume is an attempt to present some of the facts of Physiology and their applications in General Medicine in a form which fits in conveniently with pathological and clinical teaching. A complete departure from the usual arrangement of a physiological text-book has been necessary, and it will be realized that it is not easy to collect material over such a wide and varied field and yet to keep the volume within easily readable limits.

The book is primarily intended for senior students and practitioners of medicine whose busy lives do not permit of their reading more exhaustive monographs, but who are yet anxious to familiarize themselves with the physiological principles upon which so many of our modern methods of diagnosis and treatment are based.

Throughout no attempt has been made to conceal the many gaps in our knowledge, and for the benefit of those who may contemplate investigation possible lines of approach to the problems are indicated. The elucidation of some of these would in many instances add interest to the daily toil.

In the preparation of the work I owe much to many friends. My distinguished predecessor, Professor Halliburton, who has been good enough to write an introduction has read the manuscript and has been ever ready with advice and encouragement. I am also much indebted to Dr. W. H. M. Smart for the encouraging help he has given me in arranging the manuscript for the press.

The special subjects of Diatelic Tables of Sight and of Hearing have been contributed respectively by Dr. R. D. Lawrence, Miss Laura Ligertwood and

Mr. V. E. Negus, whose assistance has been of great value in making the volume more complete. I am also indebted to Dr. J. S. Macbeth and Dr. A. Hemingway for reading the manuscript, to Mr. Gilpin for the illustrations in relation to Sight and to Margaret Watson, who typed the manuscript in the first instance.

CONTENTS

PAGE

PREFACE v

INTRODUCTION xv

CHAPTER

I. LIFE AS A CLINICAL ENTITY 1

II. CONSCIOUSNESS 5
The Physical Integrity of the Cerebrum 5
Maintenance of the Blood Supply of the Cerebrum 5
The Quality of the Blood 9
Elimination of Toxic Products 10

III. VOLUNTARY MOVEMENT 12
Nervous Pathway 12
Muscle 17
Bones and Joints 18
The Movements of the Face 19

IV. SENSATION 22
The Pathways of Sensation 28
Muscle and Joint Sense 29
Taste 33

V. REFLEX MOVEMENT 35
The Axon Reflex 35
The Spinal Reflex 35
Conditioned Reflexes 41
Postural Reflexes and Co-Ordination 44
Sensory Reflexes 46

VI. EQUILIBRIUM 48
The Eyes 48
Muscle Sense 49
Vestibular Apparatus 49
The Cerebellum and Mid-Brain 51

VII. SPEECH 53
The Receptor Mechanisms 53
Association Mechanisms 53
The Effector Mechanisms 57
Aphasia 57

VIII. SOME PHYSIOLOGICAL ASPECTS OF PSYCHOLOGY AND PSYCHO-THERAPEUTICS 60
The New Psychology in Its Relation to Therapeutics . . . 65
Psycho-Therapy 68

CHAPTER PAGE

IX. Sight. The Movements and Reflexes of the Eye 72
The Cornea 72
The Aqueous Humour 73
Intra-ocular Pressure 73
The Lens 74
The Vitreous Humour 74
Refraction 75
The Reflexes of the Eye 78
The Conjunctival Reflex 79
The Light Reflex 80

X. Hearing 83
General Considerations 83
External Ear 83
Middle Ear 84
Internal Ear 87

XI. The Rate of the Heart 90
Tachycardia 94
Bradycardia 95

XII. The Pulse and the Heart Sounds 96
The Pulse 96
The Rate of the Pulse 96
The Conductivity of the Auriculo-ventricular Bundle . . 97
The Rhythm of the Pulse 98
Sinus Arrhythmia 98
Extra Systole 99
Auricular Fibrillation 100
Auricular Flutter 100
The Character of the Pulse 101
The Heart Sounds 102

XIII. The Venous Pulse. The Electrocardiograph 107
The Venous Pulse 107
The Electrocardiograph 110

XIV. Blood Pressure 113
The Heart 113
The Volume of the Blood 114
The Peripheral Resistance and the Elasticity of the Blood-Vessels 114
Pulse Pressure 117
Venous Pressure 118

XV. The Integration of the Circulation. The Effect of Hæmorrhage and Allied Conditions. The Natural Arrest of Hæmorrhage 119
The Integration of the Circulation 119
The Adaptation of Blood Pressure to Posture 121

CHAPTER PAGE

The Effect of Hæmorrhage and Allied Conditions 122
Increased Capacity of the Circulation. Surgical Shock . . 123
Peripheral Failure 123
Central Failure 124
General Considerations 126
Blood Groups 129
The Natural Arrest of Hæmorrhage 130
Blood-Vessels 131
Coagulation of the Blood 131

XVI. The Histology of the Blood 133
The Red Blood Corpuscles 133
The White Blood Corpuscles 134

XVII. Physiological Principles in Relation to Cardiac Efficiency and Disease 137
Function of the Pericardium 139
Acute Heart Failure 141

XVIII. Breathing 145
The Respiratory Centre 146
Respiratory Surface 149
Replacement of Alveolar Air 151
Mechanics of Respiration 152
The Patency of the Respiratory Passages 153
Vital Capacity 154
Pulmonary Circulation 154
The General and Cerebral Circulations 157
Cerebral Injury 158
The Blood as a Respiratory Tissue 159
The Neutrality of the Blood 160
The Quality of the Air Breathed 161
Respiratory Efficiency 162

XIX. Cyanosis and Breathlessness. Anoxæmia and Oxygen Therapy 163
Cyanosis and Its Relation to Breathlessness 163
Anoxæmia 167
The Symptoms of General Anoxæmia 170
Local Anoxæmia 171
Oxygen Therapy 173

XX. The General Respiratory Adaptations of the Body. The Respiratory Protective Reflexes 176
The General Respiratory Adaptations 176
The Lungs 176
Circulation 177
The Blood 178
Liver, Kidney and Intestine 179
Respiratory Protective Reflexes 181

CHAPTER PAGE

XXI. Physiological Principles in Feeding. Basal Metabolism . 184
Energy Supply and Tissue Repair 184
The Vitamin Content of Food 188
The Suitability of the Food for the Alimentary Canal . . . 188
Sunlight 189
Water and Salts 190
Basal Metabolism 191
The Food and Calorific Consumption of Three Normal Individuals 193

XXII. Vitamins 197
Vitamin "A" and the Anti-rachitic Food Factor (Vitamin "D") 197
Source 197
Evidence of Vitamin "A" Deficiency 198
Sunlight 198
Calcium 199
Exercise 199
Carhohydrates 199
Vitamin "A" and "D" Therapy 199
Vitamins "B" and "C" 200
Vitamin "B" 200
Vitamin "C" 200

XXIII. The Thyroid 202
Iodine 203
Excessive Calcium 204
Hyperthyroidism 204

XXIV. Body Weight 206
Energy, Intake and Output 206
Physiological Principles in the Feeding of Infants 210
The Relationship of the Endocrine Organs 211

XXV. Growth 212
Diet 212
Vitamins 213
Thyroid Gland 213
The Pituitary Body 214
Local Growth 215

XXVI. Swallowing. Digestion 218
Swallowing 218
Digestion 219
Mastication 219
Salivary Digestion 220
Protein Digestion in the Stomach 221
Control of the Acidity of the Gastric Contents 224
Movements of the Stomach 226

XXVII. Movements of the Intestines 229

CHAPTER PAGE

XXVIII. Physiological and Pharmacological Principles in Relation to Common Gastric Ailments 236
Increased Resistance 236
Interference with the Musculature and Tension 239
Irritation 239

XXIX. Blood-Sugar and Pancreatic Efficiency 246
Pancreatic Efficiency with Special Reference to Diabetes . . 249
Treatment 250

XXX. The Formation and Excretion of Bile 253
1. Hæmolytic Jaundice 254
2. Toxic or Infective Jaundice 254
3. Obstructive Jaundice 255

XXXI. The Urine 257
Anatomy 257
Quantity and Specific Gravity of the Urine 258
The Constituents of the Urine 261
Urea 262
Ammonia 263
Creatinine 263
Uric Acid 264
Phosphates 264
Oxalates 265
Excretion of Dyes 265
Diastase 265

XXXII. The Maintenance of Body Neutrality 267
Liver and Kidney 269
Respiration 270
The Intestines 270
Alveolar Carbon Dioxide and Its Significance 271

XXXIII. The Water Content of the Body 274
Thirst 275
Retention of Excessive Fluid 275
Treatment 279

XXXIV. The Temperature of the Body 283
Fever 288
Low Temperature 292

XXXV. Exercise and Rest 293
The Effect of Exercise 293
The Muscles 294
Fatigue 294
Circulation 297
Respiration 298
The Nervous System 298
Digestive and Other Organs 299

CHAPTER PAGE

The Effect of Lack of Exercise 300
The Necessity for Rest, Sleep and Interest 302
The Necessity for Variety or Interest 305

XXXVI. Protection against Disease 308
Skin and Mucous Membrane 308
Lymph Glands 309
Kidney 310
Reticulo-endothelial System 310
Immune Bodies and Lysins 310
Opsonins 311
Antitoxins 311
Precipitins and Agglutinins 313
Body Temperature, Oxygen Supply, General Metabolism . . 314
Open Air and Exercise 314
Alcohol and Salicylates 314

XXXVII. The Skin 315
Colour 315
General State of the Skin 317

XXXVIII. The Autonomic Nervous System 320
The Sympathetic-parasympathetic Balance 320
The Protective Function of the Vagus 323
Adrenaline 324
Histamine 325
Atropine 325
Pilocarpine 326
Nicotine 327

XXXIX. The Balance of the Endocrine Glands 328
The Endocrine Balance in Relation to Body Weight 331

XL. Physiological Principles in the Treatment of Certain Emergencies 336
Primary Cardiac Failure 336
Failure of Aortic Pressure 337
Failure of Respiration 339
Body Heat 341

Appendix 343
A. Carbohydrate, Protein and Fat Metabolism 343
Carbohydrate Metabolism 343
Fat Metabolism 345
Metabolism of Protein 346
Exogenous Protein Metabolism 346
Endogenous Protein Metabolism 348
Purine Metabolism 348
B. Hydrogen Ion Concentration 349
C. The Respiratory Function of the Blood 351

PAGE

On the Carriage of Oxygen 351
The Carriage of Carbon Dioxide by the Blood 354

Selected Bibliography 357

Index 365

LIST OF PLATES

PLATE FACING PAGE

I. The Efferent Paths of the Central Nervous System 14
II. The Afferent Paths of the Central Nervous System 28
III. The Nerve Paths Related to Sight 74
IV. Combined Polygraphic and Electrocardiographic Records 110

INTRODUCTION

By Emeritus Professor W. D. Halliburton, LL.D., F.R.C.P., F.R.S.

"Of making of many books there is no end." So wrote the wise men of old, but the truth of the proverb is still with us. Text-books on physiology are no exception to the general rule, but, in spite of that, I am going to give my benediction to Professor McDowall's book, and I see no reason why one should apologize for its appearance; his work is not a rival, much less an imitation, of other text-books. It strikes a new note and appeals not to the medical student when he is learning physiology in his early days but to the student of riper years, after he has been through, or while he is going through, his learning of medicine in the wards.

May I be allowed a few words of my own reminiscences. I can recollect the time I went back to physiology after I had been through the clinical mill and saw clearly for the first time how the science could help and did help the doctor, in fact, that it is what the Scotchmen used to call the "institutes of medicine." I do not suppose that this mental experience towards physiological science was peculiar to myself, many must have felt the same. I urged years ago in private conversation that the fully qualified practitioner should be one who has studied physiology after, as well as before, his study of pathology and medicine. In some sort of way this view is now being urged by others in spite of the ever-increasing burden of subjects included in what is termed the medical curriculum. Experience has taught me that it is useless to tell the second or third year student that physiology should be studied because it is the corner-stone of medicine and that it is not merely a subject the study of which is necessary to pass a certain examination and to be forgotten like a dream. The student pays no heed to such exhortations and knowing nothing of medicine regards them as oratorical platitudes. Their clinical teachers then complain that the physiological teacher has not taught them what will be of use to them in the wards. I fancy these clinical teachers are not always capable of inculcating physiological knowledge if it deals with recent discoveries and views.

My friend and successor in the chair of Physiology at King's College has evidently seen the evil and this is the corrective. I am sure the bedside teacher as well as the student will benefit from its study. My own small part in its

production has been purely consultative, but I have read and annotated every page in manuscript and appreciate its breadth of view and the clear exposition of physiological truths in the light of the study of disease. I trust it will have a wide success, for although it is not absolutely the first of its kind (others having been attempts by non-physiologists in more restricted fields), it is the one which I advise all to read.

I began this little introduction by a Biblical quotation; let me finish by concluding it: "and much study is a weariness of the flesh." That doubtless is also generally true, but I promise readers a minimum of weariness in the perusal of Professor McDowall's work.

W. D. HALLIBURTON.

CLINICAL PHYSIOLOGY

CHAPTER I

LIFE AS A CLINICAL ENTITY

You never know what life is till you die.
BROWNING.

The prolongation and amelioration of life must ever be the great purpose of the clinician. To the physiologist, its origin and nature are the greatest problems, while to all, it is a most treasured possession. Life may be considered synonymous with the power of doing something. Before the full power of doing external work is attained, the human organism passes through a series of stages during which this power of doing something is very limited. Although these stages merge into each other, some of them are of more interest than others to the clinician. At first the organism is capable only of growth, but as it becomes differentiated various kinds of work can be carried out. Of special interest is the commencement of movement in muscle, particularly that of the heart, whose beat may be appreciated at the fourth month of intra-uterine life. At this stage, however, the maternal blood supplies all that is required for growth and movement. It also takes away metabolic products of the developing organism, whose organs for the most part are incapable of such function. At the sixth month the fœtus is considered legally to be viable, for it is now capable under suitable conditions of carrying on a separate existence, though in practice this capability is not attained until the seventh month. This stage is so important medico-legally, that it may be well to summarize the evidence of having reached it. The eyelids are separated; the pupillary membrane is disappearing; the face only is free from lanugo; the nails have not quite grown to the ends of the fingers; and there is no cartilage in the ears and nose. From the sixth month onwards the child is increasingly capable of separate existence, and, by the ninth month, it has attained to full fœtal maturity.

At birth, the fœtus, now called a child, becomes responsible for its own digestion, metabolism, and excretion of waste products. In particular it is responsible for its own respiration, and evidence of air having entered the lungs is of great medico-legal significance in indicating that the child has been born

alive. There are, however, certain fallacies in this sign, but for these reference must be made to a medico-legal textbook. In England, if the child is seen to breathe, move its limbs, heard to cry, or an artery or the heart seen to pulsate, the child is considered to be alive. In Scotland, evidence of respiration or crying is required. In France, a child must also be viable. It is a curious anomaly in England, that a child born alive, say, at the fifth month, though it may not be viable, yet is still capable of inheriting property, and transmitting it (of course only in a legal sense).

Life, as a clinical entity, must be considered to centre around the circulation and respiration. In lower animals, such as the frog, the heart is capable of performing external work quite independently of any other organ. It will continue to beat for a considerable period provided it is not allowed to become dry, and its temperature remains that at which metabolism can go on. We consider that this property of contraction is inherent in heart muscle itself, which is also peculiar in that it contains large stores of energy, and, in the frog, is able to obtain oxygen from the air.

The mammalian heart, however, is more specialized. Though it has the same inherent property to beat, it will not do so except under certain conditions. It is essential that it should be supplied via its coronary arteries, with an isotonic fluid at body temperature, and at a pressure comparable with that in its aorta. The fluid must also be well oxygenated, and neutral, or very slightly alkaline in reaction. It is a fact of scientific interest, that the mere raising of pressure in the coronary arteries is sufficient to start the heart-beat, although the other factors mentioned are essential for longer action. For still more prolonged action, nourishment and hormones to assist metabolism, are necessary. A consideration of the above gives an indication of the essentials of mammalian life in its simplest form, and what conditions must be maintained if it is to continue even for a short period. If we apply these facts to the intact animal, we have, for the essentials of life (as a clinical entity), heart action, supported by body heat; blood pressure, in the aorta; adequate respiration; and the maintenance of blood neutrality. All forms of death are due to failure of one or more of these factors. Thus we see why a decapitated animal or a human being in which the medullary centres are paralysed, cannot maintain life for more than a few minutes (less than ten) after respiration ceases. Such an animal must be supplied with artificial heat and respiration. Primary failure of the body heat to an extent which will not support heart action, is only seen after prolonged exposure to cold. Failure of respiration is, however, a common clinical entity as an immediate cause of death. This will be considered in a later chapter.

If these factors are maintained, the life of the individual will continue, though it will be obvious that, to maintain these factors indefinitely, a large number of processes are necessary. Their failure, however, does not have such immediate results, although they are needed for a continued existence, which latter requires a great variety of mechanisms—for example, those required for digestion, absorption, metabolism, and their control; for the control of the water content, and temperature of the body; and for the elimination of waste products. The organs on which these mechanisms depend are all subject to disease, and may slowly result in death, as the kidney in Bright's disease, the liver in liver atrophy, the suprarenals in Addison's disease, and the pancreas in diabetes. To such a list might also be added, as essential to life, all the undetermined mechanisms which prevent bacterial infection. The higher animals, possessed of all such organs, would yet be incapable of continuing a separate existence unless possessed of the higher parts of the brain, which give them the desire to feed, and protect themselves. This may readily be shown in animals, by ligature of the carotid arteries, or removal of the higher parts of the brain, and is seen in the lowest forms of congenital insanity among human beings. Fortunately, however, there is in the body a considerable store of nourishment which is capable of maintaining the energy requirements for the vital processes, for at least two months. Even an isolated heart contains sufficient store to enable it to maintain its activity for hours. The supply of nourishment, then, is not of immediate moment in the maintenance of life, although it appears that excessive drain on the reserve may be detrimental to recovery from illness.

When we begin to consider life in a wider sense than the clinical entity, it will be found that every tissue in the body must be included. Further, when we consider life from the point of view of the body as an integrated whole, it appears to be designed for the purpose of carrying out physical work in some form or other. These mechanisms, such as circulation and respiration which we have just considered to be essential to life, are in reality the servants of the muscular tissue in so far as their activities are regulated by the requirements of the muscle. This will be more clearly seen later on. Strictly speaking, then, the clinical entity of life, as exemplified by activity of the circulation and respiration, is but evidence of the life of certain vital mechanisms without which a complete life would be impossible.

Looked at from this point of view, it will be seen how desirable it is to get away from the common conceptions of considering the body to be a mere collection of mechanisms. The proper integration of these mechanisms is as important as the mechanisms themselves. We marvel at the variety of physico-

chemical processes upon which our life is based, and our activities guided. We become painfully aware, how far the paths of civilization lead us from the purpose for which the major part of our bodies was apparently designed. It is essential that in the development of our higher mental qualities, we must not forget those physical ones which have assisted in our evolution, and which, in our time at least, will not have become wholly adapted to the comparative physical inactivity, and excessive mental activity, which modern life demands. Should we forget, too soon we shall be reminded of the words of Massinger: "Death hath a thousand doors by which to usher out Life."

CHAPTER II

CONSCIOUSNESS

It is a little unfortunate that most textbooks of physiology usually avoid a consideration of consciousness in view of the fact that unconsciousness is such an important clinical entity. Consciousness is something which perhaps we are better able to experience than define. Probably the best definition will be to consider it as the appreciation of the stream of afferent impulses which pass to the cerebrum. Although we do not know the exact nature of consciousness, we do know a large number of factors on which it depends. These factors will now be considered.

The Physical Integrity of the Cerebrum.—That the cerebrum is an essential factor is clear when we realize that any injury to this part of the brain, or its experimental removal in a higher animal, brings about an unconscious state. The reason for the unconsciousness which occurs as the result of a sudden blow on the head (known as *concussion*), and where there is no obvious damage to the skull and its contents, is not quite clear. Some hold that the mere vibration of the brain may be sufficient to interfere with its function, perhaps, putting it crudely, by a dislocation of the neurones. Others maintain that there must necessarily be damage of a more serious character, as the frequently found petechial hæmorrhages would suggest. If this were so, it would be difficult to account for those cases in which the symptoms are very evanescent, and the individuals merely feel dazed for a few moments. Still others hold that the wave of cerebral fluid caused by the blow, brings about a cerebral anæmia, according to Duret, from stimulation of the restiform bodies. It is possible that a cerebral anæmia might be brought about through direct stimulation of the vessels by the cerebro-spinal fluid, but the more detailed explanation of Duret is rather conjectural.

Maintenance of the Blood Supply of the Cerebrum.—Many of the commoner forms of unconsciousness are due to interference with this cerebral factor, and the interference may be local or general. Anything which tends to raise the pressure in the cranial cavity above that in the cerebral capillaries and veins will cause circulatory obstruction.

This is well seen in the various forms of the condition known as *compression*,

whether due to hæmorrhage, abscess or tumour. In the latter cases the symptoms may be less acute as the onset is slower and the tumour may make way for itself by destruction of brain tissue. In compression, the veins are also compressed, as is indicated by the cyanosis of those parts of the face, such as the eyelids, which drain into the cranial cavities, and the venous congestion of the optic disc. Such pressure is not, however, communicated as might appear at first sight throughout the cranial cavity, for it is prevented from doing so by the falx cerebri, and falx cerebelli. Thus, immediate death from pressure on the medullary capillaries is prevented. We can therefore realize why a cerebellar tumour may be very severe, and yet fail to bring about unconsciousness, until a late stage—after the characteristic cerebellar symptoms of inco-ordination and postural defect are well marked. This point is important, for decompression operations should be done as near the site of the tumour as possible, even if the latter cannot be removed.

The vertebral arteries supply sufficient blood to the medulla to maintain the vital centres. In an animal the carotids may be ligatured with impunity so far as the vital centres are concerned. Indeed it has been shown by L. Hill that even if the vertebral arteries of a dog are ligatured also, an anastomosis by way of the superior intercostals and anterior spinal arteries is sufficient for the adequate supply of the medulla, though the higher functions of the cerebrum are seriously impaired. The blood supply of the medulla is not interfered with until pressure is actually applied to this region. Pressure here from local causes is rare, and in the condition mentioned above it is considered that death is due not to direct transmission of pressure, but to displacement of the brain stalk downwards, causing the medulla to be compressed against the foramen magnum. This accounts for the fact that unconsciousness comes on much earlier in cerebral than in cerebellar tumours, for the latter are much less liable to cause downward pressure. Commencing medullary compression is indicated by the effect of the anæmia which brings about stimulation of the vital centres, causing a slow pulse and respiration. This latter is characteristically noisy or stertorous, from paralysis of the soft palate, and mouth muscles, due to the effect of the compression on the motor areas responsible for the control of these parts. Where the patient recovers, the compression may be looked upon as having been relieved by the contraction of the blood clot.

General circulatory conditions which affect the amount of blood supplied to the carotids will seriously affect consciousness. Unconsciousness may be brought about by compression of the carotids, and this procedure was not infrequently practised prior to minor operations in pre-anæsthetic days. It is this

fact, too, which makes accidental hanging possible. If an individual leans his head over a cord so as to compress the vessels he may become unconscious in that position and strangle himself. For this reason, too, the judicial garroting of Spain, death from cutting the throat, or from rapid strangulation may be looked upon as practically painless.

Similarly, if there be actual loss of blood, consciousness is eventually lost, but the loss of blood may be relative rather than actual. There may be an enlarged capacity of the vascular system, and the blood may become inadequate in amount "to go round." Thus, if the blood-vessels of the abdomen lose their tone, almost all the blood in the body accumulates there, and the individual faints. It is not, however, to be imagined that the loss of tone is confined to the abdominal vessels. The classical evidence indicating that other vessels are involved is that of John Hunter, who, when bleeding a man from an arm vein, noticed that the issuing blood suddenly became arterial in colour just before the patient fainted. In such instances, the actual *fainting* may be looked upon as a protective measure, for, by becoming unconscious the individual abandons the upright position, and more blood passes to the head. In the production of a sudden attack of fainting from severe pain, or a disagreeable sight, it is considered that the vasomotor centre has become inhibited as the result of the intense stimulation of the higher centres. Acapnia no doubt often contributes also (see "Shock"). On general grounds, the method of production of a faint is of considerable interest and several facts in relation to the effect of the higher centres on sensation may be significant in this respect. We know, for example, that quite a severe wound may be inflicted under conditions of emotional stress (as during a game of football) without our being aware of the infliction. If a stronger stimulation is applied, we know that minor stimulation in another part of the body is less readily felt.

We can understand then, that there may be considerable diminution for various reasons, in the extent to which afferent impulses are appreciated. It seems reasonable to believe that the vascular tone, which is maintained by the vasomotor centre, is really reflex in nature, and depends on the reception of afferent impulses. Under intense sensory stimulation there may be an "inhibition" of these afferent impulses and consequently loss of tone of the centre. This view is supported by the fact that in more emotional individuals similar circumstances may bring about inhibition of other reflex centres, such as those controlling the sphincters, or the tear sacs.

In some varieties of fainting the pooling of the blood may be understood as taking place in the skin. Fainting in a hot bath, which may have disastrous

results, is of this nature, and it is well to warn individuals liable to faint, that on no account must the upright position be assumed if an attack of faintness is felt to be coming on, but that the water must be at once let out and, if possible, the cold tap turned on. Fainting in a hot room may be considered an analogous condition. The emptying of an excessively full bladder has been known to cause similar syncope, as has also the too-sudden removal of a large quantity of fluid from an ascites or pleurisy, and the removal of an abdominal tumour, or a fœtus. In the case of the abdomen, evil results may be guarded against by the use of a binder. If a pleuritic fluid extends above the angle of the scapula it must not be all drawn off at once. Here we have also to consider the pooling of the blood in the lung which has been temporarily out of use, and the acute dilation of the heart and pericardium. Although syncope is usually evanescent, it may be fatal if the heart becomes insufficiently supplied with blood for any prolonged period. In all such cases the general pallor so often seen is due to the typical reflex constriction by which the body makes every effort to maintain arterial pressure.

The treatment of fainting and faintness is indicated by the cause. The head must always be lowered, preferably below the level of the body. If the individual is actually unconscious it is well that some gentle pressure should be applied to the abdomen, as, for example, by causing him to lie face downwards.

Faintness, or "swimming of the head" of a very evanescent character is seen in many conditions, and must be clearly differentiated from true vertigo, for the term "dizziness" is commonly applied to both conditions. In individuals with inelastic arteries, and in whom the vasomotor response to the erect posture is necessarily sluggish, faintness on suddenly getting out of bed is a common symptom. Where the arterio-sclerosis is accompanied by aortic incompetence, such faintness is still more liable to occur, and is indeed one of the classical symptoms of aortic disease. Faintness on assuming the erect posture may, however, be experienced by approximately normal people if the change of position is very rapid. Especially is this so after an enforced rest in a recumbent position, as after an illness, when the vasomotor reactions have been disused for some time.

The fleeting unconsciousness of *petit mal* appears to be best explained as a spasm of the cerebral arteries. There is a great deal of evidence that the symptom complex of an epileptic fit may be of a similar nature, and due to a cerebral anoxæmia, though undoubtedly there is a great variety of causes which may bring about the arterial spasm.

The Quality of the Blood.—It will, of course, be obvious that if the blood is incapable of carrying an adequate supply of oxygen, circulatory changes which would not normally cause unconsciousness may readily do so. Thus we see why individuals suffering from anæmia are especially liable to attacks of faintness. The oxygen-carrying power of blood depends on its hæmoglobin content. As pointed out by Haldane this may readily be arrived at clinically, by a colorimetric estimation of the hæmoglobin content, using a Gower or Haldane hæmoglobinometer. The essential principle of these methods is that the colour of the blood is compared with that of a standard (ox-blood). The standard is of a fixed dilution, and the blood to be tested is continuously diluted until the colours match. Should the blood require the same dilution as the ox-blood, the content is said to be normal or 100 per cent. If less dilution is necessary it is expressed as a percentage of what would be normal, and vice versa. In practice the ox-blood standard is better replaced by a picro-carmine, or carbon monoxide hæmoglobin standard, as in the methods just referred to.

In this relation it is marvellous how the circulation can adapt itself even when, as in some of the severe anæmias, the hæmoglobin content of the blood may be reduced to under 30 per cent. of the normal. There is in such circumstances a great increase in the heart and circulatory rate, so that the mass of oxygen required per minute may be kept supplied. There is of course a tendency to syncope if the circulatory adaptation proves inadequate, as when exercise is attempted. That such anæmic patients are conscious at all is very striking, and emphasizes the fact that the actual mass of oxygen required by the brain is very small provided the blood pressure is such that it is adequately distributed.

The quality of the blood may also be seriously reduced, if there is present in the inspired air a gas for which hæmoglobin has a greater affinity than for oxygen, as for example, carbon monoxide, a constituent of coal gas. There is, as a result of the formation of carbon monoxide hæmoglobin, a marked diminution in the amount of functional hæmoglobin, i.e. capable of transporting oxygen. Not only so, but the carbon monoxide interferes, as shown by J. B. S. Haldane, with the readiness with which the oxyhæmoglobin gives off its oxygen. There is, then, in gas-poisoning, a marked diminution in the mass of oxygen not only transported to the tissues, but also given off to the tissues of that which is transported, and the tendency to faintness and unconsciousness is very marked, although breathlessness is not evident. This latter fact is because the transported oxygen has been loaded at the proper pressure, and the hæmoglobin has been sufficiently saturated in the alveoli, and therefore is capable of keeping up

the necessary pressure in the respiratory centre. It used to be taught that the carbon monoxide hæmoglobin was a particularly stable compound. More recent work shows that dissociation of this compound of hæmoglobin will occur, so that in the event of finding an individual unconscious from gas poisoning, artificial respiration should at once be begun, if breathing has ceased, and as soon as the individual can be removed from the poisonous atmosphere. So long as the heart has not actually stopped there is a chance of recovery.

The opposite state of affairs occurs in the ascent of high altitudes. The blood is no longer adequately loaded in the alveoli, for the partial pressure of the oxygen inspired is diminished, and the respiratory centre no longer receives blood supplied with oxygen at sufficient pressure. The latter then becomes increasingly sensitive to carbon dioxide, and breathlessness becomes marked although consciousness is not affected appreciably. On proceeding still higher, or after exercise under such circumstances, the mass of oxygen supplied to the brain will become inadequate, and unconsciousness will result as in anæmia.

A similar state is produced in the unconsciousness due to asphyxia, where there is interference with the replacement of the alveolar air, or where the air breathed does not contain its proper constituents. Here, however, the accumulation of carbon dioxide brings about the characteristic respiratory distress which precedes the unconsciousness.

Elimination of Toxic Products.—In this factor may be included a large number of possibilities. In the first instance the tissue may produce toxic products or they may be ingested abnormally.

Amongst the toxic products produced by the body are those normally excreted by the kidney, by the intestine, and those keto-acids which are produced abnormally in diabetes (*q.v.*). There are also the acid products which result from normal metabolism, and which are normally utilized by the ammonia produced in the liver and elsewhere by the de-amination of the amino-acids. Thus we find clinically, that in diseases of the pancreas, kidney, or liver, or in stoppage of the bowel, consciousness is eventually lost if the condition is severe. Treatment in such circumstances consists of the elimination of the toxic products. Bleeding the patient, and the substitution of a large amount of intravenous saline for the removed blood may entirely resuscitate a patient unconscious from uræmia. Every effort should be made to activate the bowel, even if it is not the organ actually at fault. A drop of croton oil placed on the back of the tongue is most efficacious in this respect. In diabetes, bicarbonate injections and insulin therapy are urgently called for, and the patient may recover. Cases of liver atrophy, however, are hopeless from the first. Recent work on uræmia has emphasized

the importance of reducing the pressure of the cerebro-spinal fluid, the withdrawal of which brings about a great amelioration of the symptoms, especially the distressing dyspnœa. It is now fairly certain that this is not always due to an acidosis, as was first supposed, but may in part, at least, result from excessively high pressures in the arteries and of the cerebro-spinal fluid.

Toxic products ingested by the mouth have to be dealt with similarly. Alcohol must be removed from the alimentary canal, and its excretion by the skin hastened by keeping the patient warm. Poisoning by other drugs and toxins calls for action according to the danger of failure of respiration or circulation.

CHAPTER III

VOLUNTARY MOVEMENT

In this chapter is considered the movement made by a striped muscle as the result of an effort of will, and which has paralysis as a pathological corollary. For such movement to take place, it will be evident that the nervous pathway must be intact, that the effector muscle or muscles must be able to contract, and usually that the bones and joints must be capable of being moved.

Nervous Pathway.—All striped muscles, other than those supplied by the cranial nerves, are controlled by motor fibres which take their origin in the cells of the anterior horn of the spinal cord. These cells are affected by a large variety of stimuli. They may, for example, be stimulated reflexly, but, especially for our present consideration, they may be affected by impulses reaching them from the brain by way of the pyramidal tracts, and other paths that lead from the spinal cord, and it is along these paths that the voluntary impulses pass. In effecting a response they share the efferent path with the reflex arc and possibly with other paths. Sherrington has termed such a mechanism the principle of the final common path. This principle, by which the motor path is shared, is well seen in the case of the thoracic muscles of respiration which are controlled by the cells of the anterior horn in the spinal segments of the thoracic and cervical regions. These cells are controlled by the pyramidal tract, as is seen by the fact that we can breathe in a purely voluntary manner, and also by motor fibres apparently from the respiratory centre by which breathing is kept up involuntarily. Where there is some form of dual control, there must also be some mechanism for deciding priority. It has been established that the impulse which is most important for the preservation of the animal is always given priority in the final common path. Thus we may voluntarily inhibit the cells controlling the respiratory muscles, but we cannot asphyxiate ourselves voluntarily, as eventually the stimulus from the respiratory center gains priority over the voluntary impulses, and breathing becomes imperative.

The pyramidal tract arises in the pyramidal cells of Betz in the motor area of the cerebrum, situated in the ascending convolution immediately in front of the Fissure of Rolando. Hence it passes through the internal capsule in the cerebrum, through the mid-brain and pons to the medulla, where it crosses (for

the most part) to the other side at the so-called decussation of the pyramids. From the medulla it is continued downwards in the lateral aspect of the spinal cord, and gives off branches to all the anterior horns of the various spinal segments through which it passes. During its passage through the brain it also gives off branches to the motor nuclei of the cranial nerves of the other side. The neurone composed of a Betz cell and its axon was described by Wyllie as the upper motor neurone, as distinct from the lower motor neurone, which consists typically of a cell of the anterior horn of the spinal cord with its axon to the periphery.

There is, in addition, a subsidiary tract, known as the direct pyramidal tract, which does not cross in the medulla but passes down the spinal cord on its anterior and medial aspects. The fibres which it sends out to the anterior horn may be taken as crossing to the other side in the same segments as the anterior horns they supply (see diagram).

These tracts have been made out by studying the spinal cord at different stages in its development, and noting the different groups of nerves which have developed their myelin sheaths. More detailed information has been obtained by section of the tracts at different points, and by the study of the differential staining of the areas which have become degenerated. The motor fibres which have been cut off from their parent cells will degenerate distally.

Any interference with the motor pathway, either in the upper or lower motor neurone, must result in paralysis. The effect of the lesion in either neurone so far as the reflexes are concerned, will be dealt with below. Paralysis of the lower motor neurone we have seen to occur most commonly, other than from injury, or neoplasm, in the condition of acute anterior poliomyelitis or in the more chronic state of progressive muscular atrophy, in both of which there is degeneration of the cells of the anterior horn. Lesions of the upper motor neurone may occur at any level throughout its course. It will be noted that any interference with the tracts below the level of the decussation in the medulla will bring about paralysis on the same side of the body, while if the interference is above that level the paralysis will be on the other side of the body. It will be evident, however, that in cerebral conditions affecting the path low down in the pons at a level such that the fibres passing to the nucleus of the seventh nerve have already crossed, the paralysis will be crossed, that is, there will be immobility on the opposite side of the body but on the same side of the face as the lesion. A similar though rarer form of crossed paralysis may occur if the lesion is in the region of the crura cerebri, and here the ocular movements will

be paralysed on the same side on account of the relationship of the lesion to the nuclei of the third and sixth nerves.

A lesion also may not necessarily affect the whole tract, but as in the various forms of sclerosis certain of the motor fibres are more affected than others, or the lesion may affect the whole tract as in injury or new growth. Why in sclerosis certain tracts should suffer more than others is unknown.

One of the commonest forms of injury to the pyramidal tract is seen in apoplexy, in which the tract is pressed upon by hæmorrhage in the region of the internal capsule. This is the result of rupture commonly of the lenticulo-striate artery (a branch of the middle cerebral), whose walls obtain little support from the surrounding nervous tissue in this region. If the hæmorrhage is not enough to raise the cerebral pressure sufficiently to affect the vital centres in the medulla, then when the clot contracts, and the individual recovers consciousness, the interference with the path of the voluntary impulses becomes evident. The degree to which the paralysis may affect the fibres in the different areas depends on the anatomical arrangements of the internal capsule and the size of the hæmorrhage. The fibres for the face which are passing down from the lower part of the Rolandic area lie externally, and are therefore most liable to be pressed upon, and next come those of the arms (see diagram). Thus a small hæmorrhage may leave little permanent effect other than some slight interference with facial movements or speech.

Lesions of the cortex depend for their result on the exact nature of the motor area affected. As the result of extirpation, electrical stimulation and disease, it has been shown that the region is strictly situated, as already noted in the convolution immediately in front of the Fissure of Rolando. The areas for the legs are uppermost and most mesial, while, in order downwards, come the areas for the body, arms and face. It is to be noted, too, that the area concerned with arm movements is very large compared with those for the body. This is not surprising when we consider the infinite variety of movements which the arm carries out compared with the more limited body movements. The sequence in which these areas occur is of considerable importance in relation to the blood supply of the part, namely, by the middle cerebral artery which passes upwards in the Fissure of Rolando. This artery, like most of the cortical arteries, is terminal, that is, it does not anastomose with others. Any condition of blockage, due to embolism or thrombosis, is liable then to shut off the blood supply completely from certain areas, and is more likely to affect the artery towards its termination. Thus we may get paralysis of the legs

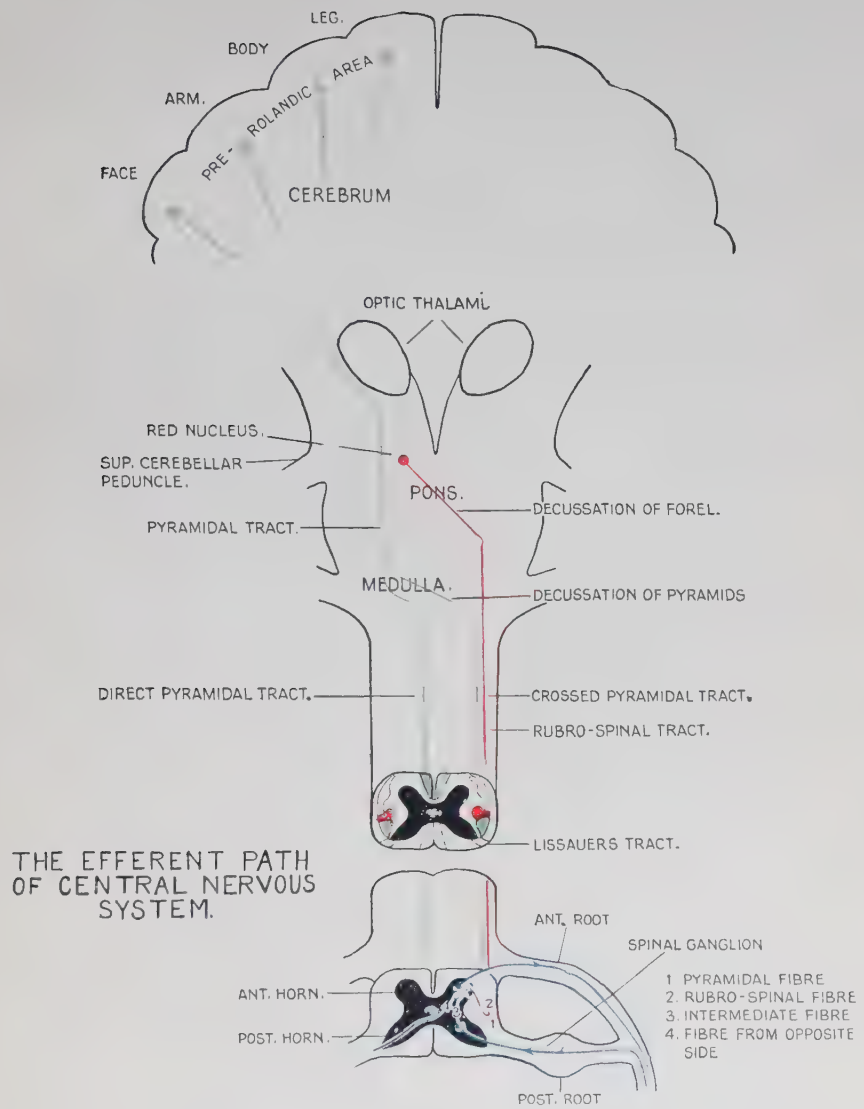


PLATE I. The Efferent Paths of the Central Nervous System.

only, although at first quite commonly the lesion is more widespread. Again the clot may block any of the branches of the artery in this region, and the area paralysed will be strictly localized. Apparently the area responsible for the motor action in relation to speech is unilateral. It is situated on the left side in right-handed persons, in the inferior frontal convolution, and is known as the area of Broca. This is dealt with further under "Aphasia" (page 57), which we now know to be a less simple condition than was formerly thought. In embolism the source of the embolus is usually evident, and is commonly an injured cardiac valve or aneurysm. Clots from the venous side are more likely to be held up in the lung. In thrombosis, in which there is local clotting, as the result of injury to the vessels, from sclerotic changes in the wall or pressure from without, the onset is often more gradual, and the effect more general, giving what is commonly called softening of the brain, although local thrombosis may occur. As would be expected from the nature of the lesion, in embolism and thrombosis (where localized) there is not necessarily any great interference with the blood supply of the cerebrum as a whole, and consciousness is not always lost.

For convenience it is desirable to consider motor movement as starting at the Betz cells, but it will, of course, be realized that this is but an arbitrary point of commencement. The stimulus which results in motor movement reaches the Betz cells from some other area of the brain. It may be held that no movement can occur except as the result of a stimulus from the outside world, usually immediate, but remote in the case of stimuli, such as pain, arising within the body itself. As Noël Paton has pointed out, "it is unnecessary and gratuitous to invoke the conception of automatic action on the part of any parts of the central nervous system."

Kinnier Wilson emphasizes the possible importance of the frontal lobes as being a higher motor area, and points out the many association fibres which connect it with the thalamus. He suggests that since the movements of chorea are obviously of a higher type than those of Jacksonian epilepsy, the cause of the former may possibly be in this physiologically superior motor area.

All that has been said of voluntary muscle does not, however, hold absolutely, as at first sight would appear. We must also consider what are known as the extra-pyramidal tracts, that is, motor tracts other than the pyramidal, which bring about movement of ordinary voluntary muscle. We shall see below that when the cerebrum is removed the muscles are in a state of excessive tone, the result of impulses passing down from the region of the mid-brain. This is further seen in the fact that postural reflexes do not depend on the cerebrum,

but on the existence of an arc through the mid-brain and upper part of the medulla. It seems obvious that there should be a motor path which can be activated from the region of the mid-brain. The best known extra-pyramidal tract is the rubro-spinal which arises from the cells of the red nucleus in the mid-brain. The afferent impulses concerned in postural reflexes and the like, may be considered to pass down this path. We have not any clear evidence of the existence of any other tracts, though there is ground for showing that efferent impulses may also originate in the region of the basal ganglia and mid-brain. These may possibly be conducted downwards from the red nucleus. More and more evidence has accumulated that many of the primitive movements of voluntary muscle are not solely controlled by the pyramidal tract. Thus we find that in conditions in which there is certainly complete loss of voluntary power of a limb, yet its muscles will still respond to some of the primitive movements associated with posture, such as standing and walking. It is said that very young children can move their limbs before the pyramidal tracts are functional. How far this may be due to reflex action on a lower level is difficult to say. Further, there is evidence brought forward by Graham Brown, showing that stimulation of the red nucleus brings about purposive movement, such as that of walking. The work of Wilson who has described the clinical signs of lenticular degeneration indicates also, that the basal ganglia may have an important function in this respect. The fact that in lower animals, such as fishes, the optic thalamus is a motor as well as a sensory area, further emphasizes this possibility. In lenticular degeneration, increased reflexes and tone are a marked feature, while the facial expression is one suggesting chronic laughter, which may reasonably be considered as an exaggeration of a primitive movement. More recently the condition of paralysis agitans has been described by Ramsay Hunt as being due to degeneration in this region, especially in the globus pallidus and caudate nucleus. In this instance there is loss of the primitive auxiliary movement, such as that of the arms in walking. Interference with the postural reflexes in walking brings about the characteristic festination, in which the individual is described as chasing his centre of gravity. This worker goes on to suggest that the impulses passing down from the basal ganglia do not use the final common path, but continue as a separate path throughout to the muscle. So far, however, the attractiveness of the possibility is its chief claim for notice, since our knowledge of this subject is still in its infancy. Kinnier Wilson remarks that it is ridiculous to assume that such a simple histological structure as is found in the corpus striatum could be responsible for the vast number of functions which have

recently been attributed to it. He puts forward much evidence to show that many of the oft-quoted signs and symptoms of striatal disease may readily be due to disorder in other parts of the brain. It is one of the subjects on which accurate clinical observation, and detailed post-mortem examination of the tissues possibly concerned may throw an enormous amount of light.

Muscle.—In voluntary movement the muscles are the effector organs and, fortunately, except in actual injury or in rare conditions, they are rarely the primary cause of paralysis. This does, however, occur in the muscular dystrophies, in which, for no apparent reason, the muscles, especially certain groups, degenerate. In the case of pseudo-hypertrophic paralysis the muscles although degenerated may appear large because of the deposition of fat which eventually replaces the fibres. In this condition the paralysis occurs in early life, and is slow in onset, by which it is readily distinguished from the more rapid acute poliomyelitis. Also in dystrophies the reflexes are not affected until the disease is sufficiently advanced to affect muscle tone; nor is there a reaction of degeneration, both of which points serve to differentiate them from progressive muscular atrophy (page 13), in which, as in acute poliomyelitis is, there is degeneration of the anterior horn of the spinal cord. Why certain muscles, e.g. the shoulder girdle and upper arm in Erb's type, or the face and later on the shoulder and arm in the Landouzy-Dejerine are affected, is as yet unexplained.

The muscles, however, may be at fault secondarily if the motor path is interfered with, since in such circumstances the muscles supplied may degenerate or may not develop. In the latter instance the bones also fail to grow properly through loss of trophic influences and also because they are not used. This condition is seen in meningeal hæmorrhage which causes the more usual "birth palsies."

More commonly degeneration occurs as a result of disease of the spinal cord or of injury to the spinal nerves and such degeneration may be of importance in estimating likelihood of recovery. When a muscle degenerates, after a brief period of increased excitability to all forms of direct stimulation, there sets in a reaction of degeneration in which the muscle, although it no longer responds to faradic stimulation, still contracts to a galvanic stimulus even to a weaker current than that which will affect the healthy side, though the muscle reacts more sluggishly. Further, in degenerate muscle the minimum stimulus which will bring about a contraction is obtained when the circuit is made and the anode is on the affected muscle (A.C.C.), while a stronger current is necessary

if the kathode is on the muscle (K.C.C.) * a condition of affairs which is the reverse of that found in healthy muscle, where K.C.C. is greater than A.C.C. It is, however, generally admitted that these reactions are often far from clear and they merge gradually into a condition in which the muscles fail to respond to any stimulus. The muscle may also become the seat of spasm and rigidity which occurs when there is a lesion of the upper motor neurone with exaggerated reflexes and loss of tone. On the other hand, if the lower motor neurone is destroyed, the muscle is quite flaccid and toneless, which, like the state of the reflexes, assists in the determination of the site of the lesion, causing a paralysis or loss of muscular movment. The condition of the muscle necessarily also affects the position of the limbs. Thus after an anterior poliomyelitis the affected limb is loose and flail-like, as is commonly also found after neuritis, which may bring about drop-wrist or drop-foot. On the other hand, the rigid limbs of a spastic paraplegia are similarly characteristic and when affecting the leg lead to a typical, spastic gait.

Bones and Joints.—It will be obvious that in order to perform the majority of muscular movements it is necessary that the bones and joints themselves should be acting properly, a fact which can be readily tested as a rule by passive movement. If this is forgotten a congenital dislocation of the hip may readily be mistaken for some sort of paralysis or a patient with an ankylosed knee may unwittingly be requested to flex the knee joint.

Finally, voluntary movement may appreciably be affected by pain, but this is usually made clear by the patient.

Hysterical Paralysis offers a strange and as yet an inexplicable problem. The individual is simply convinced that *she* (for the condition is usually met with in women) cannot make certain movements and does not. There may be complete trance or the condition may be local. For example, she may be unable to speak, yet may be capable of saying "Ah" if a show is made of inspecting the larynx. Again, she may claim that she has lost the power of moving her eyes and when she looks about she has to move her whole head. The paralysis is quite genuine and is maintained, even though the individual does not know she is under observation. Yet, if she is asked to maintain a fixed gaze on an object, and the head is moved, she can do so, which indicates that there is no actual paralysis of the optical muscles except in the mentality of the individual. Cure by persuasion, suggestion or trickery, which often requires a very keen wit, is usually possible. It will be understood that such paralysis has to be clearly

* The anode is the positive pole and the kathode the negative pole. A.C.C. is anodal closing current, and K.C.C. is kathodal closing current.

distinguished from organic paralysis, which in young people is usually less rapid in its onset and accompanied by wasting and a typical change in the reflexes. Functional paralysis is also important, as it may be grafted upon a real organic paralysis. Indeed, it is commonly so. This is often seen, for example, in disseminated sclerosis which almost invariably is improved by a short stay in hospital without any treatment, but when the functional impairment is removed the progressive organic impairment still remains.

Hysterical disturbance may, on the other hand, be of the nature of a contraction of a limb or, if in the abdomen, may have the appearance of a phantom tumour. It may also be convulsive, and simulate epilepsy, but is distinguished from the latter by the fact that there is usually a purposiveness, and the patient never hurts herself. It must, however, be realized that these patients are not feigning, but suffer from a genuine mental disturbance which is not dependent, so far as we know, on any pathological change in tissue, but rather has an emotional basis. The sensory aspect of the condition is dealt with on page 30.

The Movements of the Face.—Although these movements are in no wise different from other muscular movements in so far as they depend on the functional efficiency of certain muscles and nerves, they have a special importance in relation to medicine and surgery, in that they are largely responsible for the expression of the individual and are often influenced by general and nervous lesions.

We are all familiar with the extent to which the expression may be "the tablet of unutterable thought" (Byron), although we are at the same time fully aware how often it may be far from an index of the feelings in those accustomed to conceal their emotions. In general, however, the habitual expression of the individual does give a general idea of his outlook on life. The melancholic, and the hypochondriac, often proclaim themselves by their expression, as do the self-satisfied beings of this world. Pain, fear, and anxiety each has its facies more difficult to describe than to appreciate.

The physiology of expression is little understood, and is peculiar to the higher mammals. There are, however, indications that it is to a large extent dependent on the basal ganglia, and may be looked upon as a reflex through this region. Thus in degeneration of the lenticular nucleus, described by Wilson, there is an expression of what has been called chronic laughter. In Parkinson's Disease, on the other hand, which has been considered to be due to a similar degeneration in the corpus striatum or caudate nucleus (globus pallidus), the face wears an expressionless mask, described by some as a reptilian stare. The eyes may be largely responsible for an expression, and this is well seen

in the surprised or fearful aspect in exophthalmic goitre. Any sympathetic stimulation, such as fear, brings about dilated pupils, widened palpebral fissures, and a similar expression. But in exophthalmic goitre there is a definite exophthalmos, the exact cause of which is not quite clear. The fact that recovery from hyperthyroidism does not result in recovery from the exophthalmos suggests a more permanent cause, e.g. the accumulation of fat in the orbit.

The part played by the tone of the muscles of the face is made evident by its absence at death, or its approaching advent. The so-called Facies Hippocratica, first described by the Father of Medicine, in which the face is hollow, the eyes glazed and sunken, and the jaw dropped, is commonest at the end of wasting diseases, such as cholera and the like, where the patient dies of exhaustion. The expression, on the other hand, will be affected by excessive muscle tone, as in tetanus, where the corners of the mouth are drawn up, and produce the risus sardonicus of fixed sarcastic aspect. Here, as in strychnine poisoning, we have a reversal of the normal reciprocal innervation (see page 41). Every attempt to open the mouth is accompanied by a contraction of the more powerful muscles which close it, instead of the normal inhibition.

The normal tone of the facial muscles depends on the facial nerve, and it is an interesting anatomical and physiological problem as to the exact path of the sensory side of the arc, for it is to be presumed that the tone of these muscles, like that of others, has such an arc. The fifth nerve, which is sensory to the face, would be an obvious path, but excision of the Gasserian ganglion does not usually appear to interfere with facial tone nor with deep pressure sensation.

It would seem, therefore, probable that muscle sense from the facial muscles, passes centrally by way of the facial nerve, although this nerve is not usually considered to be sensory except in so far as the chorda tympani is concerned, and this is not really a branch of the facial nerve proper. The presence of the geniculate ganglion on the facial nerve does not appear to serve any useful purpose, unless it is to contain the parent cells of sensory fibres, since the fibres of the chorda pass subsequently as the Vidian Nerve to Meckel's ganglion, and some possibly to the nucleus of the ninth nerve. The tone of the facial muscles is profoundly altered, not only by lesions of the facial nerve, but also by lesions at or above its nucleus and of the motor area of the cerebral cortex responsible for facial movement.

Should the whole facial nerve be involved, as it may be from neuritis (due to exposure to cold outside the skull), or in the Aqueduct of Fallopius (commonly as an extension from middle ear disease), or, more rarely, between this

point and the nucleus, typical Bell's paralysis is seen in which the muscles of the whole of one side of the face are immobile and toneless. At first, the healthy muscle pulls away the skin from the affected side, but later, when degeneration of the paralysed muscle sets in, it produces the stronger pull. The diagnosis of the site of the lesion depends on the associated symptoms, especially those affecting hearing and taste. The latter is only brought about when the facial nerve is affected at the part where it is accompanied by the chorda tympani—for practical purposes in the aqueduct. Hearing may be reduced by disease in the ear, or, if the auditory apparatus is not otherwise affected, hearing may actually become more acute for low tones, by paraylsis of the stapedius muscle, which is supplied by the facial nerve as it passes through the bone.

Lesions affecting the tract between the cortex and the nucleus of the seventh nerve, the so-called supra-nuclear lesions, are commonly seen in hemiplegia. In this instance the upper part of the face escapes, and the patient can close his eyes. This may be taken to indicate that the fibres concerned with the upper part of the face are supplied from both sides of the brain. A crossed paralysis is not infrequently seen where the lesion is in the pons, and affects the fibres to the seventh nerve nucleus after they have crossed. At this point the pyramidal tracts containing the fibres to the limbs have not yet crossed. Hence the limb paralysis is on the opposite side to that of the face.

The tone of the muscles which move the jaw, and are responsible for the symmetry of the face, depends to some extent on the motor division of the fifth nerve, which, if damaged, leads to paralysis of the masseters and pterygoids. The result of this is that if the mouth is open, the jaw is pushed over to the diseased side by the healthy muscles of the other. There is also loss of perception of the high notes in hearing, from paralysis of the tensor tympani.

CHAPTER IV

SENSATION

All sensations of whatever kind are in the first instance received by the receptor organs adapted for the variety of impulse they are intended to receive. The receptors which exist in the so-called special senses, such as sight and hearing, are but nerve endings of a highly specialized kind for a similar purpose. We have, for example, quite definitely, a number of organs which respond to vibrations in the air and the ether. Some waves we appreciate as sound by the auditory apparatus; the spectrum we appreciate as various colours by our visual apparatus, while the longer infra-red waves we appreciate as heat. The very short rays, on the other hand, we cannot appreciate directly, although (as many X-ray workers know to their cost) we may become aware of their effects later. Whether all kinds of sensation will some day be shown to be due to similar vibrations, possibly intra-molecular, forms a most fascinating speculation, more within the realms of Physics and Chemistry, however, than of Physiology at the moment.

When we consider that each nerve fibre is apparently insulated from the other, it is easy to see that direct stimulation of the fibre requires a strong stimulus—as pointed out by Bayliss, the sense of touch may be brought about by a stimulus which would not be sufficient to stimulate the trunk of a nerve. The essential function, then, of special nerve endings is to produce an impulse by a degree of excitation which would not otherwise be effective. It seems probable that all the sensory nerve endings which exist in the skin have a definite specific function, but our knowledge is as yet not very accurate on this point.

In the skin we have the sensations of touch, pain, heat and cold. The sense of pressure depends on the deeper structures, and like muscle sense is served by the muscular, rather than by the cutaneous nerves. The cutaneous sensations have recently been made a subject of special study in the Clinical Institute at St. Andrew's, where it has been shown by Herring and Waterston that the heat and cold spots (long known to exist) fluctuate, that is, the exact situation of the spot varies as if to give certain regions a rest. This fluctuation may be related to the formation of certain rashes and blotches. As yet, however, it has not been ascertained on what special nerve endings these sensations depend.

Touch is known to be dependent to a large extent on Meissner's Corpuscles, which are found especially in the palmar surface of the fingers. But apart from this little definite is known.

The sense of pain is of special clinical interest. It is difficult to suppose that pain is appreciated by any special receptors, since as pointed out by Herring it would not be reasonable to assume that structures like the ureter and other viscera are provided with special receptors and special nerve fibres to meet a pathological event which may not occur for a generation. Pain can apparently be brought about by excessive stimulation of any nerve fibre, especially if the stimulus is harmful. In certain circumstances, such as after a very superficial burn, a heat stimulus which is just warm on normal skin, or if the normal covering of the nerve endings be removed, as by a blister or removal of the finger-nail, becomes exquisitely painful. Similarly, an irritant readily abolishes the sense of heat, cold and touch, leaving only pain, while again we have in central irritation, as at the upper level of the anæsthetic area in paralysis, a zone of hyper-æsthesia in which pain is very easily elicited. With such increased sensitivity of the skin as occurs after the application of an irritant, there is also a considerable loss of exact power of localization. If the nerve endings are free, as in the cornea, pain may be almost the only sensation appreciated, but in the cornea it is possible to appreciate a mild degree of sensation more akin to touch, which is capable of bringing about reflex closure of the eyelids. Similar free nerve endings occur in the skin where they may have special significance. From what has been said it will be obvious that an investigation of sensation offers a large field of work.

The cause of pain in muscle offers a special difficulty. Muscle is not sensitive to any ordinary sensation. In striped muscle the only sensation experienced, apart from ordinary muscle sense, is pain which results from spasmodic contraction, as in cramp or in the shutting off the blood supply by an embolus. In the latter instance the embolus may bring about a spasm of the arterial muscle, although spasm of the latter when it occurs elsewhere in the body, as in the fingers or retina, is not necessarily associated with pain. This matter is dealt with further below in relation to visceral sensation.

The kind of impulse set up in the special nerve ending we believe to be identical in each instance, as first enunciated by Müller in his so-called Law of Specific Nerve Energy. (The term "energy" it will be realized is not used in its modern sense.) However excited, whether directly or by way of the nerve ending, each fibre gives rise to its own special sensation and, in adults at least, has a local sign. Thus pinching of the retina or section of the optic

nerve in surgical removal of the eye gives rise to a flash of light, as does also a blow on the occipital region, which is the visual area of the cerebral cortex. Similarly, electrical or mechanical stimulation of the chorda tympani gives rise to a sense of taste.

The actual significance of the sensation depends on the analysis in the central nervous system. Crude sensation may be appreciated in the optic thalamus, from which it is distributed to the cerebral cortex, where a more refined analysis takes place. To certain areas are allotted special functions in this respect, for example, the visual area in the occipital lobe; the auditory area in the temporal lobe; or the post-Rolandic area for general sensation (Plate II). Past experience is of great importance in the appreciation of sensation. On the other hand, a new sensation, such as section of the vomer in resection of the nasal septum, cannot be localized accurately at all. We rapidly form associations round objects of a certain size and shape, e.g. a large key we expect from experience to be heavy. A small object, which requires a certain muscular effort to lift it, which is cold to the touch and hard, although it may be disguised in appearance, from past experience we may know is probably metal. This association expresses itself further in the local sign. Thus there is a time-honoured experiment of Aristotle in which an object, e.g. the nose, placed between the crossed fingers of the hand, is appreciated as two objects. The stimulation of certain fibres we appreciate as something touching the foot. Even if the leg is amputated, stimulation of these fibres in the stump will still give rise to pain referred to the lost foot. Clinically, too, it is important to remember that pain may be experienced in regions remote from the lesion. Pain in the leg simulating sciatica or disease of the knee joint may be the first indication of a condition pressing on the nerve roots higher up. This is not infrequently seen as the result of cancer of the rectum with associated enlarged glands. When the pain is of an obscure origin and is not associated with any obvious local abnormality, the whole pathway from the seat of the pain, at least theoretically, to the cortex of the cerebrum has to be considered, although if purely local the cause is more likely to be outside the central nervous system. The various crises of tabes in which the posterior roots are diseased may be looked upon as produced in this way. Experimentally in animals the painting of the sensory area of the cortex with strychnine will, as shown by Barenne, bring about sensations of pain referred to the periphery by the animal.

Referred pain, in general, is based upon a previous experience, as the sensations from each final segment have a local sign. Ordinarily we correlate sensation passing into the central nervous system, say from the thoracic region, by

any special route with a definite area of the body. The more frequent the experience the more accurately we localize it, as in the hands. If, however, the sensation is uncommon, we may have difficulty in localizing it. Thus we may have difficulty in finding a sensitive spot on the back or we may not be able to localize accurately pain in a tooth until we have ascertained that stimulation of a certain tooth brings about pain. In the case of so-called referred pain, sensation may originate in an area normally supplied by the autonomic nervous system. We are, however, unaccustomed to pain entering the spinal cord from such regions, and the pain is referred to a more superficial region which is supplied by the same root and from which we are accustomed to appreciate sensation. This conception, first suggested by Ross, has been further elaborated by Mackenzie and by Head, the latter of whom has mapped out the superficial area of the body in accordance with this idea. Thus in gallstones pain may be felt between the shoulders; the pain of renal calculus radiates down the thigh; diaphragmatic pain may be referred to the fifth cervical segment from which the phrenic nerves arise. Stomach pain is referred to the margin of the ribs, and so on. The area to which the pain is referred, may actually become tender, hypersensitive, and may even redden, although not necessarily so. Of interest too are the blebs produced in herpes zoster, in which there is inflammation of the posterior root ganglia, and a chain of blebs along the distribution of the particular spinal segment affected. Similar areas of hypersensitivity corresponding to definite nerves may occur in any part of the body.

Pottenger has made a detailed study of this subject, and furnishes a table of the distribution of pain referred from the viscera in certain diseases. These depend on purely clinical evidence and are somewhat uncertain, as factors other than the special lesion concerned do not appear to be adequately excluded. Thus frontonasal pain is described as being referred from such a variety of organs as the heart, lungs, stomach and liver, and it is difficult to conceive how this can be explained on anatomical grounds which are the essential bases of referred pain. Our knowledge of the sensory sympathetic paths is, however, as yet very small. It is, however, not difficult to see on anatomical grounds why (for example) the pain of angina pectoris which probably arises from the heart and the aorta should be referred to the shoulder and should radiate down the left arm which are all supplied by the same thoracic segments. The pain may be so intense that it may spread to another segment, as when the pain of toothache and earache are confused.

In criticizing the well-known scheme of Head it is easy to say that the superficial areas are not always found, but this must not be expected, for as

soon as the patient has learnt that a certain organ and not the superficial structure is at fault, he learns to refer the pain to the organ concerned. We have in neurotic people a similar sort of condition, in which a superficial pain, such as that of pleurodynia, is referred to an internal organ, especially if there has been any reason to suspect the latter. How often do we find a pain in the lumbar region referred to the kidneys, whatever its cause!

We see, then, why in children, whose detailed experience of skin sensation is less well developed, the site of a lesion of an internal organ may be accurately localized, e.g. McBurney's point in appendicitis.

The exact paths by which impulses may pass into the central nervous system from the viscera are not yet accurately known, but it appears that the impulses pass in with the white rami of the sympathetic rather than with the grey rami as might be expected. Stimulation of the central end of the latter causes a rise of blood pressure and reflex movement. Stimulation of organs may have the same effect, and in this way it is possible to indicate some of the pathways. The author has recently introduced a more sensitive method in which the reaction of the pupil in a chloralozed animal is taken as an index of sensation.

The paths of the afferent impulses from the heart have a special interest in relation to angina pectoris. Langley, using the reflex method, and subsequently the author independently using the pupil reaction, have found that the afferent fibres pass into the spinal cord by way of the upper thoracic segments. Evidence of impulses passing up the nerves of the neck from the heart was far from conclusive, and from this we learn that although a section of a cervical nerve, e.g. the depressor, may ameliorate the symptoms, it cannot be expected to prevent all sensation. Langley, as the above evidence indicates, recommends section of afferent rami in the upper thoracic region.

Visceral sensation, in general, is by no means so varied as in other regions. Pain is almost the only sensation experienced, although others may be appreciated by the abdominal wall. The sensations of temperature and of burning, as in hyperacidity, may be felt in the œsophagus, but it is difficult to be certain if these are felt in the stomach as spread of the temperature effect and psychological reasoning add a complication. Further, the pain is limited to special kinds of stimuli in the intestine. If the abdomen is opened under a local anæsthetic, the viscera are quite insensitive to local stimuli such as cutting, although stretching may cause pain. All visceral pain appears to be of the latter nature. Gastric pain is due to muscular spasm, possibly set up by an ulcer, the irritation of which brings about the spasm. Similarly the symptoms of indigestion are apparently brought about by pyloric spasm. The pains of

labour are of a similar nature, as are also those in spasm of the colon. According to Poulton, if a bag is inflated in the stomach, pain is experienced when the bag is allowed to empty itself. This is to be expected, as the gentle stretching such as occurs during the intake of food is not painful, whereas when the bag is relaxed the exaggerated associated muscular contraction causes a sensation comparable to the pain of hunger. How such contraction or spasm may bring about pain is somewhat uncertain, since as stated in relation to pain (see page 23), we do not exactly know what are the pain receptors. From an analogy with cramp in striped muscle, in which pain occurs when the blood supply is cut off, we may imagine that cutting off the visceral blood supply brings about similar pain. Whether or not, however, the pain arises from blood-vessels (for we know that arteries are exquisitely sensitive), or from a compression of nerve structures, or possibly the effect of lack of blood on the latter, is difficult to decide, although certainly it appears as if one of those factors was responsible.

The pain of colic, such as may occur in the passage of a gallstone, a renal calculus, or in irritation of the intestine, is characterized by its intermittent nature. This is an important fact which serves to differentiate it from inflammatory pain. The fact too, that it may be stopped by pressure is important in the same respect. Intermittency is a characteristic of peristaltic movement. Smooth muscle if stimulated electrically is found to be refractory, i.e. irresponsive to further stimulation, during both its contraction and relaxation. This may in some way be concerned in the causation of intermittency of action. Mechanical stretching is the best possible stimulus for smooth muscle, and hence the intense pain of biliary and renal colic. This fact will be referred to in relation to constipation.

Some surgeons make use of Rovsing's sign—the fact that an inflamed appendix may cause pain if distended by drawing the hand down over the descending colon.

When, however, the inflammatory condition affects the parietal peritoneum, the pain is continuous, and sometimes the surgeon may diagnose from this a retro-cæcal appendix by the nature of the pain.

The fact that the pain in appendicitis may be mostly due to its muscular spasm is very important in relation to abscess formation. When the latter occurs, and the muscle becomes paralysed by the toxin, if not actually destroyed, the pain subsides, unless the parietal peritoneum is involved. Its disappearance may suggest recovery, but in reality the patient is all the more urgently requiring surgical interference to prevent the spread of infection, and the onset of general peritonitis. Local palpation, the pulse rate, and possibly the temperature,

are then of the utmost value in diagnosis. Although smooth muscle cannot be thrown into tetanus in the ordinary way, it is nevertheless capable of entering into sustained contraction. Admittedly, we do not know the exact function of the longitudinal muscle in this respect. The normal contraction may become exaggerated to the extent of being considered a spasm. This is common at the cardiac and pyloric sphincters. Irritant conditions may also set it up in the colon, spasm of which may be intensely painful, although appreciably relieved by atropine which paralyses the motor fibres of the vagus. The colon may be felt to contract under the hand. The severe contractions of the uterus in labour are of a similar nature. Here it is evident that the tension of the muscle is responsible for the pain rather than the actual contractions, since there is no pain after delivery when the uterus may be made to contract quite hard by manual massage as is commonly done to prevent hæmorrhage.

THE PATHWAYS OF SENSATION

The impulses which cause sensation pass into the central nervous system by way of the afferent nerve fibres to the cells of the spinal ganglia, and thence to the posterior horns of the grey matter of the cord. These fibres may be concentrated in the nerve as in the case of the fifth cranial, but more commonly form part of a mixed nerve. The impulses responsible for **pain, temperature, and tactile localization** cross immediately, or soon after entering the spinal cord, to the opposite side. We know this is so because in the condition of syringo-myelia (in which there is enlargement of the spinal canal in the centre of the cord) there is a loss of these sensations in the segments affected, usually at first in the cervical region. In such circumstances severe injury, such as the burning of the fingers by cigarettes, may readily occur, unknown to the patient.

These impulses pass up the spino-thalamic tract via that of Gowers to the optic thalamus. At this point there is evidence that they can become appreciated in consciousness as crude sensation, further refinement taking place in the cerebral cortex, to which the impulse is relayed from the thalamus. Thus if the cortex is removed an animal or individual is capable of knowing that it is being hurt but is unable to localize the pain. Similarly, it is unable to distinguish between different grades of temperature. The area actually responsible for the more detailed appreciation and localization is known to be definitely the post-central convolution—immediately behind the Fissure of Rolando and on the other side of the fissure from the corresponding motor areas. This localization has been made out from the fact that in man injury or stimulation (Cushing) causes numbness or other sensation in the appropriate part. Simi-

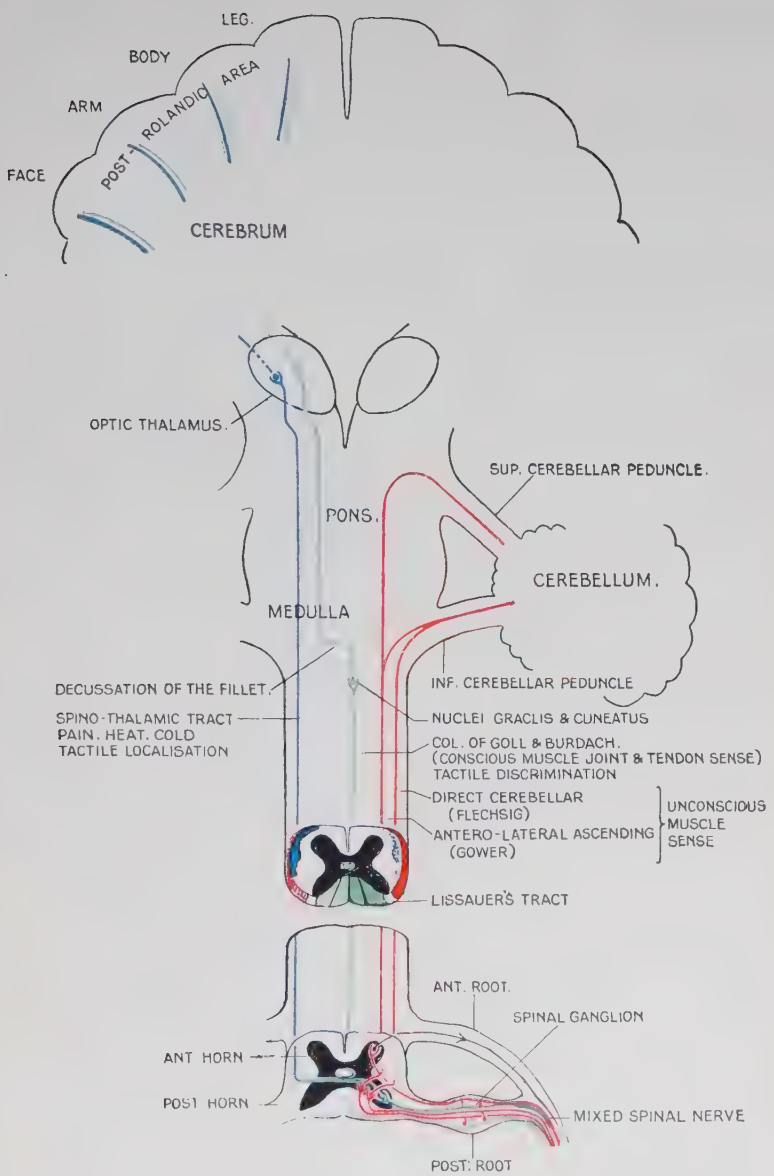


PLATE II. The Afferent Paths of the Central Nervous System.

larly in animals, painting the sensory area, which, however, is not necessarily post-central in lower forms, with strychnine (Barenne) causes the animal to have all the appearance of suffering pain in the corresponding part of the body.

Muscle and Joint Sense.—With this sense also, for purposes of convenience, is discussed the path of impulses conducting the sensation of tactile discrimination, that is the sense by which we can distinguish between two or more points placed on the skin. By muscle and joint sense we appreciate the position of our limbs where they may be placed, either by ourselves or passively. Muscle and joint sense is partly conscious and partly unconscious and is appreciated by sensory nerve endings or muscle spindles in the joints, tendons, and muscles. The unconscious sensations are those which, in the main, are responsible by reflex action for the maintenance of posture, equilibrium, and muscle tone, including that of certain organs such as the stomach and bladder.

The pathways of such impulses are quite distinct from those which carry the other forms of sensation. The impulses pass into the cord through the posterior nerve roots. Here the *conscious* and unconscious impulses take a different course. The former are continued up the cord on the side they enter, by the axons of the cells of the spinal ganglia running in the posterior columns of Goll and Burdach to the nucleus gracilis, and cuneatus respectively. From this point they are again relayed to the optic thalamus of the opposite side. The actual crossing occurs at the so-called decussation of the fillet, in the upper part of the medulla. From the thalamus there is a further relay to the cerebral cortex, like those of ordinary sensation. The thalamus acts then as the distributing centre for all sensory impulses to the appropriate part of the cerebrum. (Plate II.)

The pathway which is responsible for carrying the *unconscious* muscle sensations which are so important in relation to posture is as follows: A number of fibres from the posterior roots do not pass directly up the cord, but arborize around the cells in Clarke's column. From these cells arise the direct cerebellar tract, which lies in the postero-lateral aspect of the cord. This path is uncrossed, and passes by way of the inferior peduncle to the cerebellum. These tracts are very distinct, and may be traced by the fact that they degenerate if cut off from the cells from which they originate, namely, those in Clarke's column, or those in the spinal ganglia.

The size of the tracts in the upper parts of the cord indicate the enormous number of impulses of this nature which are conducted and their importance for the animal. An interesting explanation as to why the fibres for conscious muscle sense do not cross until they reach the medulla has been given by

Halliburton. He points out that the cerebellar tracts arise from collaterals from the fibres carrying similar muscle and joint impulses upwards. If these fibres were to cross immediately on entering the cord, they would have to recross in order to join or give rise to the cerebellar tracts of the proper side.

On these impulses depend not only posture and co-ordination, but also the senses by which we appreciate size and shape (the stereognostic sense) and weight of bodies. In these senses we really rely on the results of the associations which have been made around those of tactile discrimination and muscle sense. The clinical symptom of astereognosis or inability to recognize the qualities of an object by touch, is the result in cerebral cases of limited lesions of the superior parietal lobule (Kinnier Wilson) of the cerebrum. Lesions of the tracts leading to this region will obviously have the same effect. Evidence that stereognostic power is of this nature may be seen in the fact that if two fingers are crossed, and a thin pencil placed between them, two objects will be appreciated instead of one. This is due to the fact that normally the outsides of the two fingers are not stimulated by a single object. Similarly in judging weight we compare it with the amount of muscular movement which we remember was necessary to sustain a known weight. A similar principle is seen in the estimation of blood pressure by obliterating the radial artery with the finger when we compare it with the amount of pressure necessary to obliterate our own presumably normal pressure. A similar mechanism is at work in the estimation of the size of the object we see. We are all familiar with the various optical delusions which may result if the associations around a given movement are upset, or if the standard objects with which we normally compare unknown sizes have been altered.

From a consideration of the above, it will be evident that sensations may be interfered with in a very large variety of conditions. We have already seen that local interference will destroy the reflexes at the segment affected, and also that all kinds of impulses pass directly by collaterals or by intermediate neurones, to the anterior horns of both sides and neighboring segments. It is by these that the reflexes are brought about.

The *sensory nerve endings themselves may be paralysed* and this is brought about intentionally when we inject local anæsthetics subcutaneously. The nerve endings may also be paralysed by cold, or their stimulation impaired if the path is insufficiently supplied with blood.

The nerve paths themselves may be interfered with in their passage to the spinal cord. Thus, numbness after neuritis is common, and total anæsthesia will result from nerve section. We commonly experience such numbness if

we chance to keep up pressure on a nerve trunk such as the popliteal when we have a temporary numbness of the foot. The anæsthesia of beriberi is considered to be neuritic in origin.

The posterior roots are markedly affected in tabes. Here the degeneration may affect the spinal ganglia and the roots degenerate secondarily or may themselves be compressed at their entrance to the membranes of the cord. If the cells are affected, then the corresponding paths will be affected from the nerve ending peripherally to the columns of Goll and Burdach centrally. Muscle and joint sense is markedly affected and there are consequently disturbances of equilibrium. If a limb is placed in a certain position the patient has difficulty in placing the other limb in a similar position or he is unable to describe accurately the position into which the limb or, for example, the big toe has been put. It must, however, be noted that purely voluntary movement is unaffected and by the use of his eyes the patient may succeed in placing the two limbs in the same position. At the same time considerable destruction of tissue may occur without any appreciable sensation. Perforating ulcers of the foot or Charcot's Joints in which the joints may be entirely destroyed are strikingly painless. At the same time there is a loss of trophic influences normally dependent on the existence of the reflex arc, which is destroyed (see page 36). It is seen, too, that in spite of such structural change, its normal accompaniments such as heat, redness and swelling are absent. Similar atrophic conditions may occur in the nails and gums.

Any sensation may be affected according to the exact nature of the lesion. As the result of loss of general sensation the patient may experience the feeling of walking on cotton-wool. What is still more strange, in the "masque tabetique" of Duchenne, he may experience the sensation of having no face, when the fifth nerve is affected. The disorders of co-ordination which may result are considered in the chapter on "Equilibrium."

Considerable success has been achieved of late by anæsthetizing the posterior roots, or by the so-called para-vertebral anæsthesia, in which the results are much more localized than in the better known spinal anæsthesia where the drug is injected into the spinal canal.

Interference with the pathways in the spinal cord produces a varied result in virtue of the fact that the fibres for pain and temperature cross immediately on entering the cord, while those for muscle sense do not. We have seen that at the actual point of crossing the former may be pressed upon by an enlargement of the spinal canal as in syringo-myelia. Here, however, the effect is, for a time at least, limited to those areas, the pain and temperature impulses from

which cross at the level of the lesion. Impulses from a lower level are not affected. The latter, however, are affected by a new growth or anything which interferes with the conduction of the cord. It will be obvious, however, that should the lesion be limited to one side of the cord, the pain and temperature impulses from the same side which have crossed below the level of the lesion will not be affected, although those of ordinary sensation which do not cross until they reach the medulla are lost. Sensory impulses of pain, however, which have crossed from the opposite side, below the level of the lesion, will be interrupted (see Plate II).

It is to be noted, too, that at the upper level of the zone of skin anæsthesia, on the opposite side from the lesion, there is a zone of hyperæsthesia presumably due to a reaction at this level. This fact tends to demarcate the level of the lesion more clearly for diagnostic purposes.

In some diseases certain of the afferent paths appear to be more liable to suffer than others. Thus, in postero-lateral sclerosis there is no anæsthesia because the spino-thalamic tract lying more anteriorly escapes, while there is destruction of the more posterior, such as those of Goll and Burdach, and also the cerebellar tracts, with loss of conduction of muscle and joint sense. From the loss of the latter, muscular inco-ordination is a marked feature, and the term ataxic paraplegia has been given to the condition. The pyramidal tracts also suffer, giving the characteristic motor effects with exaggerated reflexes. Similarly in amyotrophic lateral sclerosis, although there may be considerable disturbance of sensation, there is no actual anæsthesia, the lesion being confined to the pyramidal tracts and anterior horn, especially (in the first instance) to those of the arm region. In Friedreich's Disease or hereditary ataxia the loss of muscle sense is more prominent than the sensory change. It may be that the paths of ordinary sensation which pass upwards depend on somewhat variable and less well-defined tracts, while those on which muscle sense depend are more rigidly fixed.

In disseminated sclerosis, on the other hand, in which there is a patchy sclerosis or hardening throughout the nervous system, paræsthesias, such as girdle pain, are more liable to occur, though usually the interference with motor movement and inco-ordination is the most marked feature.

In more general conditions such as the inflammation in acute transverse myelitis, the anæsthesia is complete.

The sensory change in hysteria we do not yet understand, and it offers the best possible field for enthusiastic research. Lack of sensation may be complained of by the patient or, in anæsthesia of the palate or cornea, may be dis-

covered by the physician. There is evidence that these latter are actually produced by him during the examination as the palate and cornea at other times act normally. The patient is frequently anæsthetic in a given region such as the hand as a whole, and there is no correspondence with any definite nerve supply. The disability may persist or may be rapidly evanescent. The writer has had a patient, a girl who was anæsthetic on one side of her whole body, if she lay on that side for more than half an hour. There could be no doubt whatever about the genuineness of the anæsthesia. Yet the patient was cured by trickery with a faradic current. In some instances, it will be found possible to transfer the anæsthesia from one part of the body to another with a magnet!

There can be no doubt that hysteria is closely related to the hypnotic state in which anæsthesia or any anomaly of sensation may be suggested, such as that a pebble is too heavy to hold or actually burns. The anæsthesia of hysteria may even be made to disappear in hypnosis. In accordance with Babinski it is generally believed that hysteria is brought about by auto-suggestion.

Physiologically hysteria is of interest since it emphasizes the importance of the mental attitude in sensation.

What is possibly of more consequence is the opposite condition, in which there is hyperæsthesia. When this is local it may be extremely difficult to differentiate from pain due to organic cause. Here again we find that the functional element is not infrequently grafted upon an organic condition. It is obvious that the occurrence of such a condition may have very dire results, since operations and the like may be performed in an attempt at relief.

Taste.—Taste is really a compound sensation, as it is so greatly aided by smell. Clinically, we are aware of this in conditions which interfere with smell, for even a cold in the head may appear to impair taste. Various kinds of taste are localized in different parts of the tongue, and are carried by different nerves, although in the middle part the dividing line is by no means a hard and fast one. The posterior part of the tongue is responsible for the bitter flavours, and here are situated the circumvallate papillæ, which are special receptors for taste. This region is supplied by the glosso-pharyngeal nerve, to which fibres pass by way of the pharyngeal plexus. These afferent fibres, however, pass subsequently to the otic ganglion, and the third division of the fifth nerve. Sweet and acid taste is restricted to the anterior part of the tongue, where the filiform and fungiform papillæ predominate. The anterior two-thirds of the tongue are supplied by the chorda tympani which, it will be remembered, is also responsible for the secretion of the submaxillary and sublingual glands. On reaching the geniculate ganglion, however, the motor fibres for the most part

pass across to Meckel's ganglion as the Vidian and great petrosal, and thence to the second division of the fifth cranial nerve.

The fifth nerve is then, really, the nerve of all taste, although the pathways of the sensory fibres are somewhat varied. The apparent and otherwise unnecessary association in the otic ganglion of the fibres which supply the posterior part of the tongue, with the secretory fibres of the parotid, and moreover those of the sensory path from the anterior part of the tongue with those supplying the sublingual and submaxillary glands, suggests possibilities regarding reflexes by which the saliva and sensations of the tongue are related. It will be seen below that the character of the food taken into the mouth can influence salivary secretion (page 220), but as yet no definite paths have been defined. It will be obvious from the above that the sense of taste is primarily interfered with in lesions of the fifth nerve, and its subsequent connections. The most important and commonly affected region is the chorda tympani in its passage through the Aqueduct of Sylvius.

CHAPTER V

REFLEX MOVEMENT

These are movements which we make without any effort of will and quite apart from their great physiological interest, their study is of the utmost value in the localization of nervous disease. Reflexes are amongst the most primitive movements of the body. They are primarily designed for the protection of the animal, the maintenance of posture, the supply of food, and the adaptation of the animal to its environment.

The axon reflex is the simplest form of reflex known, and is best exemplified in the case of the fifth nerve as shown by Ninian Bruce. If a blister is applied to the cheek a reddening of the skin results from dilatation of blood-vessels. This is not a direct action upon the blood-vessel, because, after the nerves supplying the part are cut, the dilatation is only obtained for a short time, and once the nerve has degenerated the reaction disappears entirely. Such section is not infrequently carried out in the treatment of obstinate neuralgia. As excision of the Gasserian ganglion does not affect the reaction, provided the nerves have not had time to degenerate, it must be assumed that the reflex depends entirely on the distal portion of the nervous connection. We know, however, that vaso-dilator nerve fibres pass out with the sensory nerves and we may assume then, that these have been stimulated, and the impulse has passed over to the efferent vaso-dilators in the nerve trunk. The advantage of such a mechanism to the animal, for the protection of its skin, is obvious. The Lovén reflexes which are probably of the nature of axon reflexes and are of importance in relation to the blood supply of organs in general are referred to on page 119.

The spinal reflex, on the other hand, depends on the integrity of the reflex arc through the spinal cord. By means of such a reflex, the sensory stimulation brings about a movement of voluntary muscle. Spinal reflexes are of two kinds, the superficial reflexes which are brought about by stimulation of the skin, and the deep reflexes, brought about by stimulation either by a blow or sudden stretching of the sensory nerve endings in tendon.

The organic reflexes, on which depends the evacuation of the bladder and the bowels, are probably brought about by a variety of axon reflex, which, how-

ever, is supplemented by a spinal reflex control. This is evident from the effect of injury to the spinal cord, and in adults by its voluntary control.

For the complete arc the following are necessary:—a sensory nerve ending; an afferent neurone to the posterior root ganglion, and from there to the spinal cord, in the case of some reflexes an intermediate neurone in the cord; an efferent neurone; a motor nerve ending, and an effector organ, usually a muscle.

Absence of a spinal reflex is an indication of interference with this arc at one point or other, and such interference may result from disease of any part of the arc. The muscle itself is seldom at fault, although this may occur in the muscular dystrophies when the condition has progressed. The nerve trunks, too, are occasionally the site of disease, as in neuritis. Usually, however, the cells of the arc are affected. This occurs in progressive muscular atrophy, and acute poliomyelitis in which the flail-like, flaccid (from loss of reflex tone) and atrophied limbs are characteristic. In both conditions the motor cells of the anterior horn are affected, and the absence of the reflexes is associated with impairment of movement and degeneration of muscle, the essential difference being that in the former the onset is gradual and the course of the disease progressive, while the latter is an acute disease, as the name indicates, and its effects remain local.

A similar state of affairs occurs in the sensory side of the arc in tabes dorsalis, where there is degeneration of the posterior nerve roots, often of the cells of the posterior horn of the spinal cord and the posterior ganglia. Here the absence of reflexes is associated with sensory impairment, and, although movement as such is unaffected, ataxy results, through faulty conduction of the proprioceptive impulses from the muscle spindles, upon which impulses co-ordination largely depends.

In some areas, such as the arm, where the normal reflexes are no longer required to any great extent, for the maintenance of posture, it is often extremely difficult to elicit reflex movement. In skin reflexes, too, the sensory nerve endings are appreciably altered by local conditions such as cold, or excessive stimulation. In others, such as the leg, the reflexes are normally more active, and their absence therefore is of more significance. In some individuals, however, the normal reflexes, as for instance the knee jerks, are by no means easy to elicit without reinforcement, such as getting the patient to concentrate on some other act, such as the pulling apart the clasped hands. The reflex arc, in general, may be depressed by conditions affecting the nervous system, as by drugs, e.g. bromides, which appear to reduce the conduction across the synapses, between the neurones of which the reflex arc is composed. Similarly, conditions

of low blood pressure, as seen in shock, bring about a marked depression of the arc.

With the disappearance of the spinal reflex, there is also loss of muscle tone, which likewise depends on the integrity of the arc. We must further assume that, for the maintenance of tone, there is a constant stream of impulses passing in from the sensory nerve endings, since section of the posterior roots of sensory nerves brings about their disappearance.

The spinal reflex is of itself a complete mechanism, capable of independent action and activity. It is no doubt concerned essentially in the maintenance of posture, and the protection of the animal. It is, however, under considerable influence from the higher centres. This is seen in the experimental removal of the cerebral hemispheres. In such circumstances the animal goes, as first shown by Sherrington, into a state of decerebrate rigidity, owing to the marked increase of tone in its muscles. All its reflexes are increased, and as seen below, some may be elicited which it may not be possible to obtain normally. Such mass rigidity occurs occasionally in disease, but more commonly for reasons described below the rigidity is more local.

Interest in the nature of such increased tone has been stimulated by the claim of Hunter, that the tone is of sympathetic origin, and the result of the contraction of tonus fibres in muscles as distinct from the fibres of ordinary contraction. That there are two such sets of fibres seems fairly clear, but the case in favour of sympathetic control must meantime be considered as "not proven." The reflex nature of the tone, and of decerebrate rigidity, is evident from the effects of experimental section and disease. For these are required the functional continuity of sensory paths from the muscles themselves to the medulla and mid-brain, wherein may be considered the apex of a reflex arc (Bazett and Penfield). The efferent path is doubtful, as indicated above, for while there is evidence of its being sympathetic, there is also evidence of its being spinal, and we are familiar with the fact that tone disappears on section of the anterior spinal roots. It is clear, however, that the reflex arc responsible for tone is depressed by the cerebrum, and Ramsay Hunt has described a duplicate set of spinal nerves in association with the extra-pyramidal tracts.

The motor impulses from the cerebral cortex, as we have stated, make use of the same paths as the spinal reflexes, and it is easy to see that impulses passing down from the higher centres affect the reflexes markedly, sometimes reinforcing, and sometimes inhibiting them. If, however, the stimulus is a harmful one, it may be extremely difficult to inhibit the reflex by volition, as in stimulation of the cornea.

Clinically, if there is any separation of the higher centres from injury to the pyramidal tracts, there is marked *exaggeration of the reflexes* below the level of the lesion. This feature is made use of as a clinical means of localization, for example, exaggeration of the reflexes of the leg (and not those of the arms) indicates a lesion, usually a sclerosis or tumour below the level of the cervical segments responsible for the arm reflexes and above the level of the lumbar segment responsible for the leg reflexes. On the other hand, if both the arm and leg reflexes are exaggerated, the lesion is above the level of the cervical segments concerned in the arm reflexes and commonly is situated in the internal capsule as in cerebral hæmorrhage, or in the cortex as the result of embolus or thrombosis. It must be realized that if the onset of the lesion is acute, as in the latter condition, there is at the time of onset a profound general shock and all reflexes may be temporarily abolished. The same thing occurs in total transverse sections of the cord. In the latter, although there may be considerable recovery of the organic reflexes concerned in the bowel and bladder, reflexes generally are seldom recovered from below the level of the lesion. It used to be thought that recovery of reflexes was quite impossible, but during the World War it was demonstrated by Head and Riddoch that cases of complete spinal section were not as hopeless as at first sight they appeared if the urinary tract and the site of the lesion can be prevented from becoming infected. The persistent loss of the reflexes was described as being due to removal of impulses which pass down by way of the red nucleus and the rubro-spinal tract.

Exaggeration of the reflexes may occur in any general irritable state of the nervous system, and their occurrence without any other sign or symptom of the disease of the pyramidal tract is of no special significance. This is especially true of the knee jerk. More importance, however, has to be placed on the less easily elicited reflexes, such as ankle clonus from sudden stretching of the tendon of Achilles, and the plantar protective reflex. The latter, which is associated with the name of Babinski, is almost absent in health, except with a strong stimulus, and its presence is considered pathognomonic of disease of the pyramidal tract. There are really two distinct plantar reflexes (Walshe). In one a gentle stimulus such as scratching the sole of the foot with the finger-nail tends to cause the toes to bend downwards, as if to grasp the stimulating object. In the other, a severe stimulation applied to the foot causes it to be withdrawn, as occurs normally when we step accidentally on a sharp object. If the two kinds of stimuli be applied at the same time, the latter, being more powerful, predominates. When there is a pyramidal lesion, this latter reflex becomes exaggerated and a gentle stimulus to the sole of the foot which normally causes

a grasping movement now causes a withdrawal, as indicated by the extension of the toes (especially the great-toe), which is the first movement seen. It will be evident that although both the flexor and extensor reflexes may be exaggerated, as usual the more important protective one predominates.

Pyramidal disease is not, however, the sole cause of the extensor plantar response, nor does the absence of such a response exclude disease of the pyramidal tracts. The extensor response, as emphasized by Hawthorne, is commonly present in coma from a variety of causes and even in deep sleep. It will be evident that when the cerebrum is thrown out of use, the flexor reflex is of no value and the protective mechanism predominates.

The same is also to be said of the jaw jerk, in which, by a tap on the chin, the jaw is jerked forward. When this reflex can be obtained there is almost certainly a lesion of the motor fibres between the cortex and the motor nucleus of the fifth nerve.

An ankle clonus, brought about by jerking the foot upwards, is occasionally obtainable in functional nervous disease, but it is characterized by not being maintained like a true ankle clonus if the pressure of the foot is kept up.

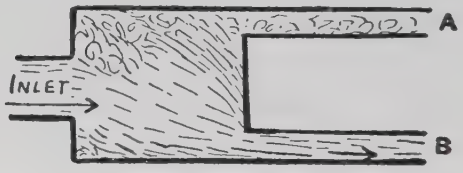
Exaggeration of the reflexes may also be brought about by the therapeutic use of strychnine, which diminishes the resistance in the synapses. A similar condition is brought about in the early stage of tetanus, and, as was emphasized in the Great War, increased tone of the muscles is seen in the immediate vicinity of the lesion before the onset of the more severe symptoms indicated below.

With the increased reflexes in destruction of the pyramidal tracts, occurs increased muscle tone which has certain peculiarities. In hemiplegia, from destruction in the internal capsule, there is commonly increased tonus in the legs, but in the arms the hypertonus is in the flexor muscles, which bring about the characteristic attitude of the arms (Feiling). Where the lesion is higher up towards the cortex, the hypertonus is less marked. On the other hand, destruction of the extra-pyramidal tracts, as in Parkinson's Disease, leads to a more generalized hypertonus affecting both flexors and extensors. This form is often found in encephalitis lethargica.

In the spinal cord, the more severe and diffuse the disease, the more likely is the hypertonus to affect the flexors. Unfortunately these facts are as yet unexplained, but they are of considerable value as an indication of the severity and possibly the progress of the condition.

Reflexes have the important characteristic that they become improved by repetition, a process which Sherrington has called *facilitation*. The passage of

the impulse through the synapse from one neurone to another is made easier by the passage of the previous impulse in the same direction. The same character is frequently seen in summation. A stimulus may of itself be insufficient to excite a response, but a succession of such stimuli eventually brings about an effect. An easier path apparently becomes formed, and the response becomes more immediate. As the rate of nerve impulse does not vary, we may assume there is diminution in the normal resistance at the synapse. That there is such a resistance is clear since the time between the stimulus and the response is longer than can be accounted for by the time the impulse takes to travel along the nerve tract. The latter time can readily be measured by comparing the time of arrival of the current of action at two points a known distance apart, in a stimulated nerve. In a mammal, the rate has been shown to be 120 metres per second. Facilitation can be imitated by causing water to run through a box of hay from which there are two openings. If flow is allowed from one exit only, the hay gradually offers less and less resistance to the flow of the water and its strands come to lie in the direction of the flow. What is just as important, however, is that by adjusting themselves to suit one direction of flow (A),



they offer more resistance than normal to flow from the other exit (B). (See fig.) There is, however, evidence which suggests that the diminished resistance is brought about by chemical changes in the synapse. The importance of this canalization process in the region of the synapse is obvious in relation to habit formation which is discussed below.

We also look upon the spread of reflexes as being influenced by the same principle. If the stimulus is strong, the response may involve the efferent neurones at several levels as the result of spread upwards and downwards in the spinal cord. If the stimulus is weak, the response remains localized. Strychnine, however, by diminishing the synaptic resistance as stated above, may cause an appreciable spreading of reflexes, as the result of stimuli which otherwise would only cause a local response.

The spinal reflex is really twofold in action, as indeed is any voluntary movement. Not only does the stimulus bring about contraction of one set of muscles but it must necessarily inhibit the antagonistic set. We owe our knowl-

edge of this subject again to the work of Sherrington who has established the principle of *reciprocal innervation.* This refers to the fact that when one muscle shortens, a reciprocal lengthening occurs in the corresponding opposing muscle as the result of diminution in its tone. Death from strychnine poisoning, or tetanus, is the result of upset of the reciprocal mechanism in which the opposing muscle instead of being inhibited becomes stimulated. Any attempt at movement, therefore, brings about a contraction of the muscles acting in opposite directions on a joint with the result that fixation occurs. As the extensor muscles are the more powerful, the fixation of the limbs is in extension. When this fixation, however, occurs in the muscles responsible for respiration, death results from asphyxia.

What has been said of the spinal reflex may also be applied to other reflexes in which there may be involved normally a large number of efferent neurones. Thus in sneezing and coughing, the sensory path is comparatively simple. In the former the fifth nerve and in the latter usually the superior laryngeal or vagus are the afferent nerves, but the efferent ones are all concerned with respiration. In this respect, the sensory cranial nerves may be looked upon as corresponding to the afferent routes in a spinal reflex.

Of a similar nature, too, are those reflexes which bring about rigidity of the abdominal wall in inflamed conditions within. Here they are obviously designed for the protection of the underlying inflamed parts, and the existence of the rigidity produced may be of great diagnostic value. In peritonitis, for example, the whole of the anterior abdominal wall may become immobilized and abdominal respiration disappear. In such a reflex, the afferent impulses go by way of the sensory nerves supplied to the parietal peritoneum and the sensory sympathetic fibres from the viscera, while the efferent paths are the ordinary spinal nerves supplying the abdominal muscles.

Conditioned Reflexes.—These reflexes are still more elaborate. The stimulus may pass to the spinal cord, but before the response is given it passes up to the higher centres where it is compared with the memory of past sensation, and the result is influenced or conditioned by past experience. In the first instance the process is a conscious act of the will, but later on requires no conscious effort.

We owe the beginning of our knowledge of this subject to the work of Pavlov, the Russian physiologist. We are all familiar with the fact that if a hungry dog is shown food it salivates freely or, as we say, its mouth waters. Pavlov showed that if a bell is habitually rung at the time of feeding, after a time salivation can be produced by the ringing of the bell although the food

is not forthcoming. It is possible, indeed, so to train a dog that it will salivate on a specific note of the piano being struck, and the animal can be taught to distinguish between half-tones in this way. Moreover, by ringing the bell half an hour before feeding, the dog may be made to salivate automatically, as it were, half an hour after the bell has been rung. In this instance Pavlov took the normal involutionary act of secreting saliva as the response and the sensory path as that of the sense of sight. Any sensation, however, may similarly be made to become the stimulus of salivation. This will be dealt with in Chapter XXVI, in which we shall see the relationship of psychical sensation to salivary and gastric secretion. A reflex of a similar nature may be produced where the effector organ is a voluntary muscle. Anyone who has been fortunate enough to be behind the scenes at a fire station in the old days of horse-drawn engines could not but be impressed by the way the horses responded to the ringing of the alarm, rising to attention and, on the opening of the stable doors, hastening unguided to their appointed places. The training of performing animals depends on similar principles, each movement of the trainer having its associated memory, usually that of food or punishment.

We must realize that a large number of our daily actions have a purely reflex character. At the same time it is evident that many natural actions of the lower animals are acquired by training as we see the mother animals training their young. A bear, for example, is taught by its mother to walk a tree-trunk. We can, to some extent, appreciate how many of our normal actions are reflex if we compare ourselves with a child or attempt to use our knife and fork in the unaccustomed hands. Learning to drive a motor-car, to ride a horse or bicycle, really means the formation of reflexes. Once the reflex is formed, the movement ceases to be the result of conscious effort and at the critical moment the individual makes the appropriate response with a minimum of delay. What, however, is most important is that even the sensory stimulus does not affect consciousness until we realize that a response has taken place. We are familiar with the fact that we fail to appreciate a repeated stimulus. When we are in a hot bath we cease to appreciate the heat of the water. A good example of the uncertain relationship of stimulus and response to consciousness is well seen in the individual who habitually travels by bus or train. His ticket is received and put in a particular place quite reflexly and without any conscious effort. Both the stimulus and the action are oft-repeated and it is expected that the ticket will be found in its proper place when needed and it invariably is. What has been said on page 40 in relation to facilitation and the analogy of the water flowing through a box of hay may be held to apply

equally to a conditioned reflex. Repetition is the important factor in its normal formation and we recognize this in the formation of habit. The Duke of Wellington is credited with having said that habit was merely something done twelve times. Once having formed the habit, however, we know how difficult it is to alter it. Indeed, it may be easier to break it altogether. Habitual smoking, and chronic alcoholism, present special difficulties in this respect and are closely allied to conditioned reflexes, but in this instance the failure to repeat in itself becomes a stimulus to repetition and a vicious circle results.

Once the reflex is established it is extremely difficult to get the impulse to flow in another channel. Thus, if a dog has established a reflex by which it salivates on the sounding of a certain note of a piano, it is no easy matter to get salivation on any other note. Indeed, the dog has to be taught all over again. In the formation of the conditioned reflex, then, in the first instance consciousness has been required, but gradually as the stimulus becomes repeated the memory area is no longer needed or sensation clearly appreciated, the final reflex has the appearance of a short-circuited edition of the mechanism by which the original movement was brought about.

The final product is a movement, the result of a stimulus, but neither the movement nor the stimulus may affect consciousness.

It has been said that habit formation suggests short-circuiting of the motor and sensory areas of consciousness, that such a short circuit between the afferent and efferent neurones may take place in the mid-brain and corpus striatum suggests itself from what has just been said, and this appears to be supported by a study of the closely-allied postural reflexes. However tempting the possibility, there is no good evidence in favour of it, indeed the evidence is to the contrary. There is another possibility, namely, that the impulses are passed through the higher centres so rapidly that they do not affect consciousness. In order that ordinary sensory impulses may be appreciated, they must be of a definite duration. Some conditioned reflexes, at least, must have a path through the higher centres since they may be made to disappear by excision of the appropriate part of the cerebral cortex. This possibility is further emphasized by the fact that an effort of the will, and the bringing together of other associated facts, may cause sensation to be recalled, although apparently it has been lost to consciousness. This is of importance to psycho-therapeutists who refer to such memories as being in the "subconscious." It may be that as a result of some canalization, an increased speed of the impulse through consciousness becomes possible. Such a statement is of course purely hypothetical, but it serves as a structure on which to hang our facts, and in view of the increasing

importance of psychology (which can no longer be denied a place in scientific medicine), some such structure is necessary that the proven facts of physiology and psychology may be correlated.

The action of drugs is of considerable clinical importance in relation to reflexes. As we have seen above, bromides have been stated to depress and strychnine to augment reflex action. At first sight these drugs are physiological antagonists, yet it is agreed that in cases of neurasthenia, for example, the giving both drugs together is of undoubted value (Bramwell). We have seen that strychnine in small doses facilitates reflex action by reduction of the synaptic resistance and it is only in large doses that there is reversal of reciprocal innervation. It has now been shown that bromides have a special action in inhibitory processes and that under their influence it becomes easier than usual to extinguish conditioned reflexes. In pharmacological doses, therefore, these drugs are not so antagonistic as at first sight appear, and no doubt in this fact lies the value of the clinical evidence referred to.

Postural Reflexes and Co-Ordination.—Many of these reflexes are closely allied to conditioned reflexes in their method of formation, in that they are largely the result of education and repetition, although the animal appears to have special facilities for their development along lines which are presumably a result of inherited facilitation along certain paths. The stimuli which bring about the reflexes are, for the most part, those which have been called by Sherrington "proprioceptive," that is, they are produced inside the body itself. In these reflexes we know that the cerebral cortex is not essential. For example, if the head of a decerebrate cat, i.e. one from which the cerebral hemispheres have been removed, is bent forward, the tone of the muscles in the foreleg alter to permit of flexion, as would occur normally when the animal drinks. Many other examples could be given of similar automatic mechanisms by which tone in different parts of the body is influenced by movement in another.

In the postural reflexes the sensory stimuli are received from the muscles themselves together with those from joints, tendons, the labyrinth, and from the eyes. The necessary co-ordination is brought about by the mid-brain and medulla—a fact which is extremely interesting in view of the fact that the mid-brain of fishes (optic lobes) are so well developed.

That the cerebellum is not so important as has been thought has been clearly shown by the school of Magnus in Utrecht. The maintenance of a balance under various conditions which depends on these postural reflexes is dealt with further in relation to the maintenance of equilibrium (page 48).

Closely allied to postural reflexes are those of "co-ordination of voluntary

movement" which are controlled by the cerebellum. The exact part played by the latter in relation to such reflexes is not quite certain, but that its function is closely concerned with the correlation of afferent impulses is evident from the existence of well-defined afferent cerebellar tracts. The existence of acquired reflexes of this kind may be readily appreciated if we attempt to use a pen or pencil with the unaccustomed hand.

For the present purpose it is interesting to note that the functions of the cerebellum may be taken over by other parts of the brain, such as the cerebrum. This would appear to indicate that the cerebellum has been specially developed in relation to the mid-brain for the purpose of co-ordination at a lower level than the cerebrum. If the cerebellum is removed in a dog, the animal loses its power of co-ordination, but eventually it recovers control and it appears that under such circumstances the cerebrum can take over the function. This observation is important in relation to the removal of cerebellar tumours, for even if the cerebellum is largely destroyed, the patient may hope to recover his co-ordinating powers. It is, however, especially interesting to note that this organ is intimately connected with the mid-brain in the region of the basal ganglia. This fact suggests that its development is associated with the formation of reflex arcs in this region, these giving responses that otherwise would require conscious effort, which is thus spared. We know that the movements normally controlled by the cerebellum can, of course, be carried out, as the result of mental effort. In the treatment of tabes in which there is interference with the conduction of muscle and joint sense as the result of disease of the posterior nerve roots, it has been shown to be possible to re-educate co-ordination by causing the patient to practise walking along a floor on which the position in which the feet have to be placed is marked. The results of such treatment and of the experiments on the dog quoted are significant, as indicating that the normal reflexes of co-ordination and possibly some of those of posture may be reproduced in a way similar to conditioned reflexes. Similarly, too, we may consider special feats of balancing by acrobats as due to a like process.

But most postural reflexes are not the result of education. A child will of its own accord assume the erect position which requires a considerable amount of co-ordination, and this may be said even of a congenital idiot incapable of being educated. From this we may presume that by the process of evolution certain paths become laid down, and conduction through the synapses connecting certain neurones is easier along some than others. Thus, too, we may explain how certain family characteristics of gait may become evident, although by a process of training they will disappear. One is tempted to compare what may

be called inherited posture reflexes with the "Ego" (or inherent self, of the psychologist), and the reflexes of posture and co-ordination produced by training, with the self produced by education. It may be that we have a thought mechanism analogous to motor co-ordination, and the effect which inherited mechanism can have on educated mechanisms and *vice versa* are strictly comparable. On the efficiency of the reflexes of posture and co-ordination depends equilibrium. Since disturbance of this is an important sign, it is treated later on in a separate chapter.

Sensory Reflexes.*—The reflexes with which we have just dealt are those in which the reception of a sensory impulse results in some form of activity. Knowing what we do of the formation of reflexes, the possibility that motor movement may in certain circumstances result in sensations of an analogous reflex nature can no longer be ignored. For example, an individual has a condition which causes pain on movement. The condition clears up, but pain on movement remains. That often this pain is quite genuine there is little doubt. Yet the fact that it is often caused to disappear with amazing rapidity by treatments which can have no possible influence on the local condition indicates the possibility of its reflex nature. Clinically such cases abound, although of course they cannot readily be reproduced artificially in animals. Here we are on the borderline of psychology, and in this borderland lies a vast amount of medicine and, alas, a vaster amount of unscrupulous quackery. For our present purposes, it must be realized that often no amount of verbal persuasion will convince the sufferer that there is no pain. Often a show of violent treatment such as that commonly adopted by osteopaths and chiropractors, some of whom claim that they reduce a dislocated spine (in itself an alarming diagnosis) is strikingly efficacious and suggests very much methods which we know to be necessary in altering conditioned reflexes or even habits. It remains for clinicians to work out more carefully this aspect of the subject. It is impossible to have seen the effect of a pilgrimage to Lourdes, or the collection of crutches and bandages and splints at an Eastern shrine, and not be impressed with this aspect of curative art. The fact that so many successful cults, such as chiropractic osteopathy (using the term in its original American sense), faith healing, Christian Science and Couéism flourish in our midst indicates the necessity for a real study of the subject. Medical psychology, the scientific counterpart of these cults, meantime struggles for recognition. Its acceptance

* This conception of the formation of sensory reflexes analogous to motor reflexes is a purely personal view which appears to go a long way in explaining what are undoubted facts. Similar phenomena may also be observed in pet animals which have been injured. So far as the author is aware the view has not been put forward elsewhere.

is undoubtedly hindered by its unfortunate tendency to alienate itself, especially in its language, rather than to ally itself with what is straightforward physiology, when so much could be gained by co-operation. Time alone can bring mutual understanding.

CHAPTER VI

EQUILIBRIUM

The maintenance of equilibrium depends on a larger variety of factors than is generally recognized, and these are reasonably clearly defined. Briefly, they may be summarized, as afferent impulses from the eyes, vestibular apparatus, and organs of muscle and joint sense, the paths by which these impulses are conducted, the mechanisms by which they are co-ordinated, especially in the mid-brain and cerebellum, and the motor paths by which co-ordination is brought about. This presupposes the efficiency of the muscle, bones, and joints. The above factors are now dealt with, in so far as they are clinically important. It is interesting to note that the number of impulses actually passing centrally appears to be an important factor.

The Eyes.—Here we may consider that the extent to which objects which may be focussed is the important factor, or the regularity with which these impulses are received, although individuals vary in the extent to which they use their eyes. In the majority of individuals, however, a reduction in the number of, or confusion in, such impulses brings about a distinct feeling of giddiness. This is experienced if one attempts to cross a plank bridge, look over a high place, or at the movement of a river from a bridge, and, in some people, even watching a train start. It is not, however, necessarily experienced in an aeroplane as there are numerous near objects which can be focussed. This is also well seen on climbing the Eiffel Tower, where one becomes much more giddy on the first platform, than further up, since at the higher level it is more difficult to avoid seeing the under-structure. Further evidence that it is the focussing of objects which is concerned is seen in the fact that the instillation of atropine, by paralysing a combination, is liable to bring about a loss of equilibrium. Patients so treated may find themselves suspected of being under the influence of alcohol. Similarly, in diplopia, due to inco-ordination of the extra-orbital muscles, and when the proper convergent movements associated with accommodation are rendered impossible, giddiness is common. The fact that in this condition it is not abolished by covering the eyes, suggests that afferent impulses from the muscles are concerned.

Muscle Sense.—That muscle sense plays a large part in the maintenance of equilibrium is seen by the fact that if the number of afferent impulses from the muscles is reduced, the eyes become more important for equilibration. Thus it is usually impossible for an individual to stand steadily on one leg, with closed eyes, although there may be no difficulty in doing this with the eyes open. Advantage is taken of a similar difficulty in Romberg's sign in which is tested the patient's power of standing steady with the feet together and the eyes closed. When the afferent impulses from the motor organs are diminished, as in tabes, or after severe peripheral neuritis, unsteadiness results. Similarly in tabes, closure of the eyes when bending forward, as in washing, may cause the individual to fall forward, and not infrequently damage himself from coming in violent contact with the taps of the lavatory basins. The dizziness experienced by some individuals in suddenly going from a hard pavement to an india-rubber pavement is of a similar nature.

Under conditions where there is a reduction in the number of ocular sensations equilibrium may be maintained by the addition of muscle impulses and a feeling of confidence given. Thus an individual who is quite giddy at looking down from a height is not so if he holds on to something, and has no difficulty in climbing a ladder or a tree provided he looks at objects he can focus easily.

In the same way ataxic individuals may walk reasonably steadily by making more use of their eyes and, of course, it is in these persons that the effect of closure of the eyes is best seen. The ataxia itself is the result of loss of muscle sense, for the patient can no longer adjust the exact extent of his muscular action, and the stamping, or hen gait, is very characteristic in many conditions affecting either the posterior roots, or the postero-lateral column.

Vestibular Apparatus.—It is well known that removal of the semicircular canals in animals, as first carried out by Flourens, or disease of the canals, results in a loss of power of equilibration. We now know the otolithic cavities to be responsible for our appreciation of the position of the head and the work of Breuer and Crum Brown in 1875 shows that the semicircular canals are responsible for the sense of rotation. The canals, three in number, lie one in each of three mutually orthogonal planes, each with an ampulla or enlargement at the end where it branches off from the common vestibule. In each ampulla, and in the otolithic cavities, is a crista surmounted by sensitive hairs which are stimulated in the former instance by movement of the endolymph, and in the latter by calcareous granules contained in the cavities. Excessive movement of the endolymph, such as that set up by rapid turning, will upset the normal mechanism, and giddiness from this cause is well known. Impulses pass from

the cristæ by way of the vestibular part of the eighth nerve to the mid-brain and thence to the same side of the cerebellum.

Labyrinthine disease, or destruction of the afferent path by a lesion such as an abscess, will bring about loss of equilibrium with a tendency to fall to the diseased side, for all afferent impulses responsible for equilibrium are, so far as we know, uncrossed. Vertigo of a similar nature is seen in Ménière's disease, which is also characterized by vomiting and deafness, the exact nature of which is unknown.

The semicircular canals have a special relationship to the movements of the eyes, as pointed out by Ewald and finally elaborated by Bárány, whose eye tests for vestibular function are in general use. This relationship is seen in the production of nystagmus, a short rapid oscillation of the eyeball, with a more rapid movement in one direction than another. If an individual be rotated to the left with the head erect, nystagmus to the right results from relative movement of the endolymph in the opposite direction. This cannot, as a rule, be observed. When the rotation ceases the inertia of the endolymph tends to cause it to continue flowing in the same direction, and causes a so-called after-nystagmus to the left. The existence of this after-nystagmus and its duration is an indication of the functional efficiency of the canals, each of which may be similarly tested by moving the head so that the canal is in the plane of rotation. Nystagmus may also be induced by injecting hot or cold water into the ear as a result of movement of endolymph caused thereby. In health it should be induced in 20 to 40 seconds, although the period is reduced in hyper-excitable individuals and increased in reduced excitability.

The exact relationship between the canal and the eyes is not at first clear, but it seems likely that the nystagmus is merely evidence of a mechanism by which successive objects may be focussed during movement of the head. As recently shown by Magnus and de Kleijn of Utrecht, if the head of a decerebrate animal is moved from the vertical, the eyes are retained in the vertical plane by an automatic mechanism of correction. This has been subtly expressed by Sherrington as "a cat is the right way up because the world is the right way up, and Nature arranged that it must always be so." It is usually considered that if the head is moved, there is a lag of the eyes which is exaggerated in the experiments of Magnus. There is, relatively, a movement of the eyes in the opposite direction, so that the object looked at will remain in view. The sharp movement in the direction of the head rotation is a cerebral correction. It is evident that during movement both processes are automatic, and the purpose of such a mechanism is to enable a series of objects to be seen. Every-

BOSTON MEDICAL
OCT 14 1963
LIBRARY

thing seen has to be accurately focussed on the retina for a definite period before it is recognized. If the body turns round rapidly vision would be blurred, but for the fact that certain objects are focussed and others omitted. When we travel in a train which passes rapidly through a station, we are conscious of having seen only a portion of the things to be seen on the platform and have omitted others. In such circumstances there is a rapid jump, as it were, from each focussed object to the next, the period during which the object is focussed being approximately that between the jumps. This form of nystagmus may be seen if we observe the eyes of a fellow passenger who is looking out intently from the window. The more rapidly the train is moving, the more rapid will be the jumps, provided he is looking intently, that is, he is using the cerebral correction to the full. Similarly, the more imperfect the vision or illumination, the longer must the image be focussed on the retina, and the more obvious must the jump become. If the defect is habitual the movement of the eyeballs may persist even when the individual is not moving but is merely attempting to move his eyes, and the oscillation will be brought out best when he attempts to look to his maximum extent to one side. Miner's nystagmus is considered to be produced by habitual working in a poor light, but upset of the co-ordinating mechanism may obviously lead to varieties such as the rotating nystagmus which bear no relation to the essential functions concerned. It is often seen in disseminated sclerosis, and is no doubt due to a sclerosis of the tracts by which co-ordination takes place. Its presence is often useful in differentiating between organic lesions and functional conditions, for it cannot be produced voluntarily.

The Cerebellum and Mid-Brain.—It used to be considered that all the afferent impulses were co-ordinated in the cerebellum, but more recent knowledge from the Utrecht School has emphasized the fact that the mid-brain and the brain stem even down to the upper part of the medulla play an important part in equilibrium. For complete clinical equilibrium it must not only exist in posture, but also during movement. The brain stem appears to be responsible for the former, the cerebellum for the latter, facts of considerable clinical importance, as tumours of the stem will simulate tumours of the cerebellum, although in the latter the loss of equilibrium will be more marked during movement. Sherrington has described the cerebellum as the chief ganglion of the proprioceptive mechanisms. That this is so is evident from the effect of total or partial ablation in animals, or in disease in man. Cerebellar abscess and tumour are the commonest conditions of that organ. Since impulses passing to the cerebellum are uncrossed in their upward path, we expect the lesion to

be on the same side as the symptoms. These are general weakness, and loss of tone of the muscles concerned, for we have seen that the reflex cerebellar arc is affected by cerebellar impulses, probably by way of the rubro-spinal tract. There is also asynergia, or lack of smoothness of movement, which tends to become broken into its component parts, and astasia or difficulty in sustaining an effort requiring co-ordination. In unilateral cerebellar conditions, therefore, the patient tends to fall to the side of the lesion, although if the paths to or from the cerebellum have been affected there may be some variation in its situation and intensity. The ataxia of tabes may be looked upon as partly due to the interruption of such paths.

It seems likely that the loss of equilibrium which accompanies loss of consciousness, is due to the loss of the functions of the cerebellum and mid-brain, just as the unconsciousness is due to loss of cerebral function.

In alcoholism, probably the commonest cause of loss of equilibrium, the early "light-headedness" suggests a paralysis of higher centres of appreciation of all kinds, although later the drug depresses the activity of all nerve tissue.

Impairment of muscle, bones, joints, or motor tracts may also bring about a difficulty in maintaining equilibrium. Here also there is difficulty in performing voluntary acts. Where there is only a weakening, due to cerebral tumour or abscess, it will be evident that in such cases the patient will tend to fall to the opposite side of the lesion, if the main crossed motor pathways are involved.

CHAPTER VII

SPEECH

Of recent years much controversy has raged on the subject of speech and aphasia, and while many of the older conceptions require to be modified, much of the evidence is by no means so contradictory as at first sight might appear. In the present chapter speech is considered in its widest sense, namely as the mode of interchange of ideas between our fellow-creatures.

Speech may be looked upon as depending on three distinct factors—the receptor mechanisms, association mechanisms, and the effector mechanisms. Failure of any of these will result in impairment of the power to reply to a particular variety of stimulus. A deaf man cannot respond to the stimulus of spoken words, nor can one with a diseased larynx respond by speech. When the loss of speech is due to a central cause the term *aphasia* is used.

The Receptor Mechanisms (*Afferent Projection System*).—Although normally the receptor mechanisms are those of hearing and seeing, any kind of sensation may be utilized. We are familiar with the fact that in the education of the blind use is made of the sense of touch. The peripheral mechanisms of hearing and seeing have already been described, and their nerve paths traced as far as the cerebral cortex in the temporal and occipital lobes respectively. In close association with the visual and auditory areas are association areas wherein appear to be analysed and stored the memories of visual and auditory words. It must be understood that there is no hard and fast distinction between the receptor and receptive association mechanisms.

Association Mechanisms.—Our knowledge of these mechanisms is as yet comparatively crude and while it is not as yet possible to define accurately all the anatomical areas in which these functions take place, many facts which have been collected from the study of disease are of great clinical and physiological interest.

We may consider the association mechanisms as being of two kinds: the *receptive* which lead from the receptor mechanisms to conscious understanding, and the *expressive* which lead therefrom to the effector mechanisms. As we shall see, we have indications of the pathways used by some of these two association mechanisms, but unfortunately we have not a glimpse of the nature

of conscious understanding although we can appreciate it. When, then, a stimulus of a spoken or written word is received through a receptor mechanism, it is first dealt with by the *receptive mechanisms,* which decide its significance to the individual. This significance will obviously depend on the previous associations which the individual has for the particular stimulus. Language is but a convenient conventional association of ideas round certain sounds and symbols which certain groups of individuals find convenient for the purpose of interchange of thought.

When it is desired to communicate with a fellow-creature, utilization is in the first instance made of the *expressive association* mechanism, by which certain sounds, symbols or movements which have a conventional significance are chosen, the actual speech being carried out by an effector mechanism. This mechanism, on the other hand, is merely a final common path which may be utilized for several purposes. For example, some of the muscles which produce speech may be utilized for other purposes such as mastication.

The method by which associations may be formed round certain sounds and symbols is of some interest as it forms the basis of early education.

In learning to speak, a child at an early age associates certain words with certain objects which he sees. Gradually also he begins to imitate the sounds he hears, although not necessarily understanding their meaning, and eventually learns to make sounds which he associates with certain objects. These sounds are not infrequently as a result of difficulty in pronunciation, often a travesty of the words attempted, and may be retained for a long time even when articulation is fairly complete. The sounds are symbols for the object or desire, and subsequently they are put together in sentences. Later, by practice and by education, the sentences become more grammatical.

When the child begins to read and write, the symbolic nature of speech becomes still more evident. In the first instance, a written representation of the sound is learned, and subsequently this is imitated. Gradually everything with which the individual has come into contact is capable of similar written symbolic representation, although it may be some time before the proper conventional method of spelling is acquired. Further, as the development of an individual in modern civilization is so closely associated with the possession of a facile method of communication with his fellow-creatures by means of speech, it becomes impossible to differentiate clearly between the development of speech and of intelligence. It will be evident that if the receptor or effector mechanisms are inadequate for the development of normal speech, the intelligence will tend to suffer. We have seen that in the development of speech, the associations

of reading and writing are, as it were, superimposed on those of hearing and speaking. Impairment of the former does not interfere with the latter, since the individual may have a fully-developed mechanism by which he can communicate with his fellows in a normal fashion. Loss of hearing will result in loss of speaking, as in the deaf mute, and must seriously interfere therefore with reading and writing, so that he is deficient in all the normal mechanisms of communication. As emphasized by Shaw Bolton, deafness is then a much more serious impairment than blindness from the point of view of the intellectual development of the individual, and we are familiar with the fact that those blind from birth are much more intelligent than those congenitally deaf.

The above must be considered as speech in its simplest form, since at the same time associations are made round other sensations in relation to speech. A child, for example, may have had certain experiences which have resulted from its neglect to say "Please" or "Thank you."

It is probable that the above indicates only what we may call elementary intellectual development since we know that more advanced association may not proceed in such a sequence. We may associate any sensation with an object and different individuals appear to have special facilities for association in relation to different sensations. This is well seen in the learning of anatomy. Some find dissections most useful; to some, diagrams are quite adequate; to some, descriptions; some prefer mnemonics to aid their memory. On the other hand, some find in memorizing that repetition aloud or writing down is of most value.

A similar variation is seen in the various methods by which different individuals learn a foreign language, and we may expect that the effect of a given lesion will depend somewhat on how the language has been learnt. In the case of Chinese, the written symbols do not refer to the spoken language, but to objects or ideas. A localized lesion has been known to blot out completely a foreign language.

It seems reasonable to believe that the extent to which memories of reception or expression are made use of in intellectual development may vary appreciably and thus it cannot be expected that destruction of any particular part of the brain will result in a constant degree of mental impairment.

The degree of association which takes place depends on the stress of the moment and the speed of reply. If time is given, we may bring a whole host of memories to bear on a given question, while the more elaborate mechanisms of speech, such as those concerned with correct grammar and sentence formation, may also have to be consulted. It can indeed with some justification

be held that in the power and speed of association of ideas in general depends the general success of individuals in a civilized community.

There is yet some uncertainty as to the anatomical region in which the speech associations take place, but there is general agreement that in right-handed persons it is normally situated on the left side of the cerebrum, within a well-defined cortical region extending from the posterior part of the lower frontal lobe by the island of Reil to the temporal and lower parietal occipital region (after Kinnier Wilson), i.e. what are generally looked upon as the areas of Broca and of Wernicke. Of this region it is also clear that the anterior part is concerned with expression and the posterior with reception.

Of special interest is the situation of the speech association areas on the left side of the brain. It is considered that the preponderance of the mechanism on the left side does not occur until the child is taught to write. With the use of the right hand, the left side of the brain becomes essential, although it is important to note that even in right-handed persons there is evidence that the right side of the brain is also used. No doubt the process is facilitated by the custom of previous generations to use their right hand in writing.

The regions responsible for the associations of reception occupy a wide area. In front of the visual area in the angular gyrus is the region responsible for the associations of sight, such as reading, and close to the auditory area, in the temporal lobe, are regions responsible for the associations of hearing. Since lesions of this area are fairly common, e.g. abscesses from the ear, it has been possible to localize these associations more accurately. Syllables are held to be dealt with by the first or upper temporal convolution, the posterior part of which is also responsible for grammar and syntax. The names of objects appear to be stored in the second and third temporal convolution, minor lesions of which give rise to paraphasia, in which mistakes are made in the use of words. Such detail suggests that in close association to the regions responsible for sensation generally, are areas in which are stored the associations of such sensation. We have already noted that lesions of the parietal lobe are likely to cause astereognosis (the loss of the power of recognition of form of objects), which is really loss of the associations of touch. Certain associations have obviously closer relationship than others, e.g. those concerned with reading and writing, and it is to be expected that a lesion of the visual association area will affect writing and spelling.

In relation to expression, the area of Broca, just in front of the face area in the ascending frontal convolution (i.e. in front of the fissure of Rolando), may be looked upon as being responsible for associations in relation to spoken

speech, although since the work of Marie it is no longer held to be wholly responsible for speech. Similarly, in front of the arm area is a region responsible for associations connected with writing (Buchan). It was originally considered by Broca that the area associated with his name was wholly responsible for speech, and we owe especially to Marie the recognition of other areas responsible. Few, however, will go as far as Marie or Moutier in denying that Broca's area has not a special significance in relation to spoken speech, indeed there seems to be abundant post-mortem evidence to the contrary.

It is emphasized by Kinnier Wilson that excluding the area of Broca, macroscopic without microscopic evidence is insufficient. This area may be affected secondarily from a lesion elsewhere.

In criticizing cases it has also to be remembered that although we look upon the left side of the brain as that primarily associated with speech, it is not to be understood that the right side has no function in this respect. This statement is particularly true in relation to the receptive associations. We can, for example, hear words with the right side.

When the form of expression has been decided upon, the stimulus is passed to the more executive mechanisms in the Rolandic area.

The Effector Mechanisms (*Efferent Projection Mechanism*) are normally those of spoken or written words, but any motor movement may be used. We are familiar with the use of the dumb alphabet, while in certain circumstances an expression of the face or movement of the head is as truly an effort of speech as the spoken word. Normally a shake of the head is accepted as an indication of negation, quite as emphatic as the word "No." Indeed, it may have the added significance on the part of the speaker that it is not audible. More usually, the impulse passes through the cells of the left cerebral cortex, from which fibres pass down to the nuclei of certain cranial nerves governing the movement of certain of the head and neck muscles, or to the anterior horn of the cervical and dorsal regions of the spinal cord which govern the movement of the hand in writing, or those of the chest in speech.

Aphasia.—This is a symptom, not a disease, and during the last few years there has been a tendency to enlarge the significance of the term. For practical purposes it may be considered to refer to impairment of the powers of expression and appreciation of language. From a consideration of the above, we can realize the possible mechanisms which may be at fault under such circumstances.

The *effector mechanism* proper is impaired when there is destruction of projection fibres in the internal capsule or lower, from cerebral hæmorrhage.

Such a destruction may cause a paralysis of the part of the face and tongue and affect only the actual articulation of words (anarthia) just as a paralysis of the arm may affect writing. A similar paralysis may occur in the case of destruction of that part of the Rolandic area responsible for such movements, as in hemiplegia, due commonly to embolism or thrombosis of the branches of the middle cerebral artery, lesions which usually affect also the associations.

The *association mechanism of expression* may become impaired from cortical or transcortical lesions which cause what in the past have usually been known as motor aphasia. Typically with impairment of these mechanisms there is loss of the power to express adequately, although there is no appreciable loss of understanding. In the case of loss of voluntary speech, there is not necessarily any interference with the effector mechanism, as is shown by the fact that the patient has obviously full powers and full use of structures employed normally in articulation. He may also be able to articulate accurately the words he can say, and not infrequently a patient may still be able to speak "reflexly." He may, for example, say poetry, express sudden emotions by speech, as in swearing, or he may be able to repeat to order. How this is possible is a very interesting problem and many of the ideas are little more than speculations. It has been suggested that for such automatic speech, the right side of the brain is brought into play, that only certain pathways converging on that part of the Rolandic area responsible for speech are affected, or that short cuts have been laid down at a lower level as the result of repetition. With regard to the site of the lesion, it can merely be said with due consideration of the evidence of Marie and of Moutier that in a lesion in the region of Broca's area, such expressive aphasia is usually found. A lesion immediately in front of the arm area will similarly be liable to cause loss of power to write.

Lesions in the Receptive Association Areas result, as would be expected, in loss of the function of the particular region affected. As will be understood from the diverse nature of receptive associations, a large variety of symptoms may be produced. Further, as indicated in relation to the temporal lobe, associations are scattered over a wide area, and it is therefore possible for lesions to be produced which affect certain associations, say, of hearing, leaving others untouched. Word blindness or word deafness are amongst the better known results of impairment of the regions responsible for the association of vision and hearing, but there may be produced simply a failure to name objects or to speak correct grammar. In this latter connection it is interesting to remark the association of grammar with hearing rather than with expressive side. In some

cases the individuals recognize words but do not know their meaning. Their own language in print becomes like a foreign one.

It is impossible to deal with all the results of lesions which may occur. Clearly not only may there be cortical destruction, but any impairment of the transcortical fibres joining different associations may bring about very diverse symptoms. Even the same lesion in different individuals cannot be expected to produce a similar detailed effect. Especially is this true of the intellectual state. Head, however, has succeeded in showing that there may be a considerable degree of mental impairment. No doubt we all develop our more elementary associations in the same order. He draws attention to the fact that the more recent associations are most readily lost, or they may cease to be used intelligently. Head has differentiated the varieties of aphasia as disorders of symbolic thinking, and has shown that such factors of speech as the appreciation of the meaning of words (apart from the saying of the word), the formation of sentences, grammatical construction, and so on, may all be separated in aphasia of different degrees of severity. It is doubtful if these have any practical bearing, although of extreme interest in a study of the mechanism of the formation of speech. It must also be remembered that in diseases affecting speech other motor movements, such as those of the arm and leg, are commonly impaired and the aphasia may aid in the localization and throw a light on the possible nature of the lesion. The degree to which aphasia may be recovered from in a severe case is remarkable, and there are indications that in such circumstances the right side of the brain may take over functions which normally belong to the left, and various attempts to re-educate the opposite side of the body have been made.

Lesions of the receptive mechanisms proper need only be mentioned for completeness. The loss of the sensation for general purposes is obviously the predominating symptom.

CHAPTER VIII

SOME PHYSIOLOGICAL ASPECTS OF PSYCHOLOGY AND PSYCHO-THERAPEUTICS

The extent to which Psychology has been divorced from Physiology is to be deplored, and the loss of touch brought about by their separation, although it may have been of some advantage to Psychology, has at the same time been a loss to all concerned. Experience during the Great War convinced even the most antagonistic, that Psycho-therapy in its wide sense, was a procedure of profound curative value, although the principles on which it was based might not be generally accepted. We do not disbelieve the existence of synapses between the neurones of the spinal cord, although we cannot see them, since we have evidence of their properties and their effect on reflexes. We cannot associate reflexes in matter so far as the details of synapses are concerned. It is the purpose of this chapter to indicate that though we cannot as yet definitely associate mind and matter, yet we have much evidence that the mechanisms responsible for habits of thought are not essentially different from those responsible for habits of movement, and it will be agreed that our conduct in society depends on our habit of thought acquired, and possibly inherited.

We have seen that there are three grades of reflex phenomena: the axon reflex, involving the peripheral nerve only; the spinal reflex, requiring a sensory organ, an afferent neurone, a spinal centre, an efferent neurone, and an effector organ; and the conditioned reflex, which is a still higher type, involving past experiences. The latter requires for its formation, in addition to what is needed in the spinal reflex, afferent and efferent pathways through the spinal cord, a storage of memories associated with sensations, and an analysing mechanism and association fibres to bring together the sensory, memory and motor areas of the brain. Gradually, however, the memory area is no longer required, and the sensation is no longer clearly appreciated, the final reflex having the appearance of a short-circuited edition of the mechanism by which the original movement was brought about.

The final product is a movement which is the result of a stimulus, but neither the movement nor the stimulus may affect consciousness. Many, indeed most, of the movements which we perform daily are of the nature of subcon-

scious movements, or, if we dare to introduce psychological phraseology, movement of the subconscious, as for example, the way we hold our umbrellas, the way we use our handkerchiefs, and what we do with our bus ticket. We expect to find it in the place we are in the habit of putting it, but should we be wearing another coat, we may have difficulty in finding it. The ticket has been put in a certain place as the result of a series of stimuli which have made little or no impression on consciousness. Now this formation of habit of movement is at first a simple conditioned reflex, and is like a reflex in every way. In the first instance we had a definite reason for placing the ticket in a certain place. In the formation of habit, or of movement, we apparently have a diminution in the synaptic resistance, for we know that the resistance of the synapse is largely responsible for the time taken to respond. By means of the reaction-time apparatus it may readily be shown that the reaction-time to a certain stimulus becomes appreciably less with practice. In the chapter on "Reflexes" a physical analogy to this facilitation has been put forward.

It has been said that habit formation suggests a short-circuiting of the areas of consciousness. It may be that there is such a short circuit, but it is also possible that the impulses pass through consciousness too rapidly to be appreciated. The possibility of a short circuit is rather suggested by the fact that we know that many of the higher acquired movements, especially those of co-ordination and posture, which become apparently reflex in nature, are dependent on the mid-brain, cerebellum and corpus striatum. There is evidence that these movements may, as in paralysis agitans, be seriously interfered with without affecting the higher centres. We are possibly inclined to forget the extent of our educated movements, but we are forcibly reminded if we attempt to write or use a knife and fork with the unaccustomed hand. Further, we know that the functions of the cerebellum in relation to such co-ordination may be taken over by other parts of the brain. This observation is important, as it appears to indicate that acquired movements and co-ordinations may in the absence of the cerebellum bear a very strong resemblance to conditioned reflexes, the sensory stimuli being largely derived from the muscles, joints, and tendons.

On the other hand, the fact that removal of the appropriate part of the cerebrum causes a loss of conditioned reflexes, suggests that the impulse is not really short-circuited, at least not wholly so. We know that the more delicate analysing mechanisms, which are essential to some conditioned reflexes, only exist in the cerebrum, and disappear if the latter is removed. It may be that the impulse becomes so facilitated in its passage through the cerebrum, that

it fails to be appreciated, just as we know that any frequently repeated stimulus fails to enter into consciousness.

The above deals with ordinary motor functions, but before passing on to a consideration of thought, we must deal with what may be called an intermediate action, dependent on the action of certain groups of muscle, namely speech. Speech may be the result of conscious thought, just as is movement of the legs, but it may also be the result of what has every resemblance of being a reflex. A dog may develop a reflex or, as we say, is taught not to bite when it is teased, but if the stimulus is strong enough, the animal will bite and the movement has every resemblance to the other protective reflexes. So it is with speech. Speech may be calculated, indeed it should as Shakespeare says in the advice of Polonius to his son:

Give thy thoughts no tongue,
Nor any unproportion'd thought his act.

We are, however, familiar with the statement that he or she has "spoken too quickly," and it may be at the same time, has acted too quickly, that is without having brought into consciousness a sufficient number of associated ideas.

Thus also swearing becomes an uncontrollable habit. When well-established it is quite unconscious, and gives no relief to the feelings, as it might to one less hardened. Such a mode of speech is quite clearly reflex, and is an indication of a cycle of thought, possibly involving definite pathways which have been laid down in response to definite sensations at an earlier date. The individual who does not take the advice of Polonius "gives himself away," as we say. He gives to others an undue insight into his thoughts. In other words, he has thoughts, the result of definite stimuli which have been appreciated by the senses. We see, then, that rapid expression of opinion may often be but a conditioned reflex. In the first instance, on receiving the stimulus in the form of a question, it is taken into consciousness, compared with the memory of past sensations, and the reply is given. But if the cycle of thought is formed, then, like a conditioned reflex, it is no longer referred to memory or consciousness, and hence the answer is very rapidly given, "without thinking." A dog which salivates on the perception of a certain sound, or a horse which takes the wrong turning, may justifiably be considered to have had some previous association with that sound or turning. The dog has presumably pleasant sensations of feeding associated with the sound. Similarly, the horse has most likely pleasant sensations of rest connected with a particular direction.

If they were unpleasant it would be difficult to get the animal to take that

particular turning. So it is with rapid speech. The response gives away the previous association, and hence the value of rapid cross-examination in the witness-box. Similarly, if we are writing anything uninteresting, we are apt, unless we concentrate, to interpose words of the matter of which we are thinking. Thus, too, examination papers, if quickly written, are an indication of the associations which the questions bring to the writer's mind, and not necessarily the results of his more profound powers of thinking. It is notorious that individuals good at examination papers may be incapable of original thought. In this sense, the rapid writing of such papers is largely a reflex phenomenon, affected by all those things which normally affect reflexes. For example, they may be speeded up by strychnine, a favourite constituent of tonic mixtures before examinations.

Habitual and original thought are quite distinct to the extent that voluntary and involuntary walking are. Yet they merge into one another, and the comparison appears to be strictly analogous. Habitual thought depends on previous experiences, and on how similar stimuli have been responded to. A system of memory training, such as Pelmanism, is efficacious in that it forms associations of value around certain words and ideas which can be readily got at reflexly. Our whole system of education and appointments depends on similar elementary facts. We expect that the response given by an individual to certain stimuli will be influenced by what he has been taught, or made to think, or do. It is presumed, for example, that we absorb unconsciously some of the attributes and habits of our fellow co-workers and of our masters.

We have dealt with the association of movement, which we look upon as reflexes, but when we consider thought, we find that it, too, can be considered largely a reflex. Some conditioned reflex movements we may look upon as movements of the subconscious. Habit or associations of thought are similar actions on the part of the subconscious.

But having started with pure Physiology, we find ourselves unconsciously emerging into the realm of Physiology. Here we find considerable changes in terminology, but there is no real difference in the way of thinking. Psychology is a true science, but it has suffered greatly at the hands of those who attempt to explain it without a basis of physiological principles.

Every movement we make is the result of a stimulus, and so is every thought. We hold up a book because we want to read it, we want to read it because we have heard or read something about it; and so on backwards. Thus there is always a stimulus prior to response however original we think we are, and although the original stimulus may not be appreciated. The stimulus and the

movement need not affect consciousness, indeed habitual sensations do not, for example, when we take a hot bath. After a few minutes the part of the body not submerged does not feel the water warm, unless it is moved about. Now amongst the stimuli which are more or less habitual are those from the primary instincts of self-preservation, of the herd, and of sex. Each has a definite response. The instinct of self-preservation may be at times antagonistic to that of the herd. In war time the instinct of the herd became triumphant and found its response in patriotism, but the response of sex is often rendered impossible by modern social standards. Psychology shows that under these conditions the normal responses become repressed, and the habitual response becomes altered, but, like any other reflex, although in the first instance the stimulus and the altered response were conscious acts, they gradually sink below the threshold of consciousness like a habit, where they cannot be recalled any more than the stimulus which made us form a habit.

When there is a conflict or antagonism between the desires or instincts, such as occurred in war time between that of self-preservation and of the herd, it appears that very disagreeable experiences may be disregarded and apparently forgotten voluntarily. They have, however, a "scar," for they may be shown to be still giving rise to stimuli from a subconscious level. It would almost seem that the stimuli passed so quickly or with such an intensity through consciousness that they rapidly pass beyond voluntary recall.* In other instances the individual is unable to handle the conflict, and suicide results. These matters are incompletely understood, but since the War there has been a wonderful advance in the elucidation of these conflicts and repressions, with enormous benefit to the victims. The time is not far distant when psychology of this kind will play an essential part in the training of the medical man.

The above conception of thought does not at first sight leave room for what is popularly known as "originality." This is a strange, undefinable entity, and one often misapplied. An individual who has been trained in any special subject, habitually looks at any new problem from the point of view of his training, and since the elucidation is then often obvious, he is said to be original. In reality it is quite the opposite. It may be held that the spirit of inquiry (the parent of originality) is really a habit born of the individual in that he had to suffer or fend for himself in his youth. The contrary is also well known, namely

* That it is the intensity of the stimulus which is responsible is suggested by the fact that it is possible to stimulate a nerve so strongly that there is no motor reponse. A human being can stand an electric current of E.M.F. 10,000 volts through his body, although the passage of one at E.M.F. 500 might be fatal. The subject may also be closely related to kronaxy.

the striking want of originality of purpose which characterizes those whose adult life is closely similar to that of their childhood. It is noticeable that most of the greatest personalities are those whose lives have been subject to changes of circumstance or domicile.

In art, too, at first sight, originality is apparent. A study of the rise and fall of definite schools of art, and the causes which have brought them about, readily suggests the influence of habitual thought affected not infrequently by the economics of the time. The rise of the famous Dutch School, with Rembrandt as its outstanding exponent, in relation to the fashion for painting groups of the civic guards (themselves an outcome of the Spanish wars), is a striking example of this point. When also we study the lives of the great musicians, we cannot but be impressed by the influence of their environment and family tradition. To what extent heredity itself may play a part is a difficult problem to decide. That it does play some part will be admitted in the popular mind, but accurate evidence is very scanty.

We are, it is true, faced with the problem of the genius, or of the individual who is a mathematician, but useless at classics, or *vice versa*. The difficulty is not insuperable if we believe, that as obvious physical structure can be inherited, so can the as yet hidden physical arrangements on which the facilitation of reflex acts, such as gait, and associations depend, and that those characters are subject to the ordinary laws of heredity. We do indeed popularly admit that a child takes certain mental characteristics from his ancestors. We say that certain arts run in families, and we admit that a generation may be passed over. Unfortunately, it is only when an individual has reached a certain eminence in his subject that he is remarked upon. These qualities may have been present in his ancestors, although they did not come to light, and we know how often circumstances, economic and otherwise, may affect mental development. Keith has pointed out that the qualities necessary for academic success are nothing more than those of a really good housewife and the structure of our brains shows no demonstrable improvement over those of our illiterate ancestors. There we must leave this fascinating problem.

The New Psychology in Its Relation to Therapeutics.—The position taken up by many prominent students of normal and abnormal psychology is that in the present state of our knowledge any attempt to explain mental processes in terms of physiological and anatomical data is doomed to failure. It is said, in effect, that no advance can be made at present in the elucidation of psychological problems if one tries to discuss "nerve cells" and "ideas" together: that physiology and psychology must be kept strictly apart: and

that a knowledge of the true relations of mind and body is not yet to be attained.

This idea has been especially fostered by the disciples of what has come to be known as "The New Psychology." They found that by ignoring entirely all anatomical and physiological data they were granted a new freedom, and were enabled to put forward hypotheses which carried them much further towards an understanding of abnormal psychological processes than had been dreamed of by older workers.

It is undoubted that the New Psychologists have accomplished work of the utmost value. The names of Freud of Vienna, and Jung of Zurich are most associated with the advances recently made in the study of morbid mental processes, by the use of conceptions not obviously governed by physiological and anatomical controls. Many of the views held by this school are too sweeping and apparently too revolutionary and far-fetched, to be adopted by the majority, but the fundamental principles of the New Psychology are of such immense practical value in enabling one to comprehend the symptoms found in the psycho-neuroses that their usefulness can hardly be questioned. In such abnormal states, these principles can so frequently be demonstrated, and their results so accurately foretold, that it seems presumptuous to cavil meantime at their apparent lack of physiological and anatomical foundations. With all due deference to pure physiology, it must be realized that the detailed anatomical basis of such a well-known physiological entity as a conditioned reflex is as yet most imperfectly known. It is the object of this chapter to show how matters psychological may be studied without quite ignoring physiological laws, and to indicate some of the basic conceptions of modern psychology and the laws governing the present practice of psycho-therapy.

At any given moment of our waking life we are aware of a constant stream of stimuli of great variety which reach us by means of the different organs of special sense. We have a constant awareness of our surroundings. We see, hear, smell, taste, and touch continuously; we have various pressure sensations on different parts, and we have associated thoughts, ideas, and images. All these stimuli flow along continuously and make up consciousness.

We are all aware, that just beyond the threshold of this consciousness, there lies a vast store of mental pabulum into which we can dip whenever we wish. Some portions of this store are more accessible than others, but we feel that if we try hard enough we can extract material from very remote corners. This store is made up of countless records of facts, experiences, wishes, hopes and fears. We pause a moment and are then able to recall what we were doing

yesterday afternoon. We remember the people whom we met, and as a result a whole stream of associated memories may flood into consciousness.

If the ever-changing momentary awareness referred to above be called the conscious mind, then this tract just over the threshold may be termed the "fore conscious."

Modern psychology goes a step further, however, and postulates another region of mind much wider than the last, which is called the unconscious mind—or, briefly, *the unconscious.* In the unconscious throng the apparently forgotten things of our lives, the records of impressions received in childhood and infancy and even, some hold, imprints of impressions received by our forefathers.

By no amount of puzzling or thinking can we go through the partition between the fore-conscious and the unconscious. All the content of the unconscious is locked away and cannot be exposed by any of the keys of ordinary thinking. Yet all day and every day our behaviour towards our environment is being profoundly modified by the trends and the forces and the desires of this portion of our mind, of which we are quite unaware.

We are asked to accept this as a hypothesis. Many reasons, good reasons, have been given to show that the unconscious is no myth, but its existence cannot be proved. The hypothesis is, however, worthy of serious consideration by all who would understand something of the underlying cause of many of our daily thoughts and actions, and of many of the symptoms of the psycho-neuroses and the psychoses. It should be tentatively accepted because it is a conception which explains satisfactorily a great deal of what was formerly inexplicable; because by means of it we are often able to look for and find hidden causes of deviation from the normal in behaviour; and because it is the basis upon which many highly successful methods of psycho-therapy rest.

The mind is looked upon as being made up of two systems—a primary and a secondary. The primary system has full sway during infancy and its whole tendency is to seek immediate gratification for the individual. It seeks pleasure and avoids pain, it is quite unhampered by any moral codes of behaviour. As age advances the secondary educatable system becomes imposed upon the primary, and the child learns to modify his desires. He finds that although he has instincts which demand gratification, it is often unwise, inconvenient, or wrong, that this should occur. All the time this is taking place, however, the old primary system persists. The latter, which we call for convenience, the unconscious, therefore, is to be looked upon as a purely ego-centric portion of our mind which is overlaid by the realms of the conscious.

In connection with reflexes, it is seen that reflexes are the response to stimuli

which may or may not have been analysed in the brain and compared with memory of past stimuli and responses. In pure psychology we have apparently a very similar mechanism by which a stimulus, not only of ordinary sensation, but even of thought, may result in another thought or conception. The stimulus itself may be a thought. Hence we have a thought-cycle, which we know as a *complex,* and there is evidence that this complex may exist without the knowledge of the individual. That moral and educational training, together with past experiences, will affect both conduct and thought is generally accepted, provided the response is within the conventional range of normality. Yet when the conduct of thought is outside this range, some are loth to admit that similar buried complexes outside consciousness may be responsible for the abnormality. Thus a man has been known to take a fit on riding on a tramcar which investigation showed to be brought about by the sound of the trolley wheel, which reminded him unconsciously of the sound of a shell which had almost killed him, although the man himself did not consciously associate the two sounds. The sound, apparently, brought about an unconscious cycle of thought which made him terror-stricken. But when the two sounds were brought to his conscious thought and the significance explained, the man made a complete recovery. Thousands of such cases are on record.

Many are prepared to accept the possibilities of such abnormal complexes as a consequence of war, but find it more difficult to accept what might be described as the civil corollary of such cases. Thus a man may not have obtained a much-coveted appointment, or a woman a much-desired attachment; the conscious self forbids a frank avowal of the failure, but the cycles of thoughts remain and the emotion may find an outlet in some other form more acceptable to the conscious self and the world. A psycho-neurosis may result, and, as in hysteria, a very large number of pathological conditions may be simulated and not infrequently the symptoms bear some symbolic reference to the cause of the condition. Our moral, social, altruistic and herd-obeying selves do apparently recognize the unconscious, but they may refuse admission to all the anti-social trends to which it constantly gives rise. Under such circumstances the unconscious may succeed in expressing itself and appearing under various ingenious disguises, as symptoms, dreams, or thoughts affecting conduct. The excessive enthusiasm displayed by maiden ladies in relation to the keeping of pets is admittedly of this category.

Psycho-therapy concerns itself (1) with the elucidation of such complexes by psycho-analysis and bringing them to consciousness and thus causing their disappearance; or (2) in simply breaking the cycles of thought or "the chains

of causation" of symptoms, by persuasion and suggestion, although the actual causation be unknown.

In *psycho-analysis* an attempt is made to get an idea of what is going on behind the conscious mind which the individual is encouraged to allow to pass into abeyance for a time. This may be done by asking the patient to allow his mind to wander and to name the various items which pass through his mind as he does so. That is the method known as free association. Slowly the mind will be found to drift into the direction of buried complexes. In day-dreams we have ourselves experienced such wanderings and we realize that they almost invariably lead towards the desires or fears of the unconscious self. It must be understood that they do not necessarily lead only to those complexes which are the cause of the condition being investigated.

Again, the patient may be asked to name the first word which occurs to him when another word is mentioned. Thus cup will be followed by saucer, man will be followed by woman, but if the cause of the condition is man, then there may be some distinct delay in giving the allied word, and the time taken to respond, measured by a stop watch, is found to be appreciably increased. Obviously considerable experience in the choice of words and the interpretation of the result is necessary and requires a great deal of skill.

The analysis of dreams is yet another method which may be utilized. It will be readily agreed that our dreams do bear some relation to matters which we have in our mind, but they are often fantastic distortions or caricatures, especially of our desires. Many a golfer dreams of stupendous drives or of finding a limitless number of golf balls. But even in a dream, consciousness may still exert its influence over the unconscious complexes if the latter are unacceptable to the conscious moral code. They may then appear in a disguised form. Thus a man may dream of attending a funeral of some one who is standing in the way of his advancement, although his conscious self would be repelled at the idea that he was wishing for the individual's decease. But, as we have said, the unconscious self is purely ego-centric and has no such scruple. A dream may indicate fears as well as desires. After reading a blood-curdling story we may subsequently dream that we are one of the characters of the story. In the psycho-neuroses, a habitual disagreeable dream may then be an indication of an unconscious fear, which possibly may be at the root of severe symptoms which may seriously interfere with the normal life of the individual and may lead to his confinement in a mental hospital.

Even although the underlying cause of the ailment is unknown, it may still be possible to break the chain of causation by *persuasion or suggestion.* An

individual may have a wound which he imagines paralyses his hand although the nerves and muscles are found to be intact. It becomes therefore necessary to persuade him that the paralysis is not really due to injury. Commonly, there is a definite reason, although *not necessarily a conscious one,* why the patient does not wish immediate recovery from his malady. It may be found necessary for the immediate purpose of treatment, to explain that the present inability is merely due to disuse. Diagrams and X-rays may be necessary to assist the argument, and a vital point in this method of treatment is that immediately following such explanation the patient must be made to use the limb to some extent. In persuasion, however, one stakes everything on one's power to convince the patient that there is no real reason why the disability should continue, and, if successful, the result is immediate.

The breaking of the chain of causation by suggestion is a much safer procedure from the point of view of the physician. Here is introduced a chain of thought which is incompatible with that causing the symptom or the chain of causation. Many other diverse aspects of suggestion, the prestige of the doctor, the nature of his instructions, have their effect not only on the patient directly but also through friends, and assist in reinforcing the suggestions which the physician makes. Suggestion is generally admitted to be most successful in children, the debilitated, the tired, and fortunately also in the hysterical, who have indeed suggested their own symptoms to themselves. The suggestion is often much more effective when associated with some striking, especially physical, form of treatment, and here, alas! is the realm of much quackery, as the treatment rather than the suggestion gets the credit for the cure. Space does not permit a full discussion of this point, but it is well known by all those practised in the art of medicine.

See also page 46.

The suggestion may, however, be made during hypnosis, when the conscious self is in subjection, and during which the suggestibility is greatly increased. It is possible during hypnosis not only to effect the diagnosis, differentiating, for example, between a hysterical and actual paralysis, but also to elucidate the causal complex, and to introduce chains of thought which bring about the recovery.

It will be realized that persuasion and suggestion, although breaking the chain of causation, may not necessarily do so permanently, for these chains tend to become repaired. As would be expected, therefore, the psycho-analysts are distinctly antagonistic to this form of treatment. Complete psycho-analysis, however, resulting in the complete elucidation of the chain of causation of a

symptom, is often a laborious procedure. Not infrequently the analysts are biassed along certain lines especially those of Freud which are not necessarily correct for the given case. Since very often persuasion and suggestion, assisted by time, are followed by a permanent cure, they must be considered more than justifiable.

What has been given above is but the merest outline of psycho-therapeutic principles. Their appreciation has opened up a new era in Medicine. They have bridged over the old gulf between sanity and insanity, and have already rescued many lives from chronic invalidism or lunacy.

The author is fully aware that many psychologists and psycho-therapeutists may find it impossible to subscribe fully to the views put forward above, all the more so as there is much disagreement among psychologists themselves. Many adhere strongly to Freudian conceptions, in which sex is held to play the principal part in the production of abnormal psychical states. It is often quite striking how young psychologists, at first antagonistic, become adherents to these conceptions. On general physiological grounds such views appear quite unnecessary, and are to many revolting. The author has, therefore, endeavoured to put forward the principles of the subject without any bias, except that of physiology, on which they seem to be founded.

CHAPTER IX

SIGHT. THE MOVEMENTS AND REFLEXES OF THE EYE

With the Co-operation of LAURA M. LIGERTWOOD, M.B., F.R.C.S. (Edin.)

The sense of sight arises through impulses received by the brain as a result of the action of light upon certain specialized nerve endings in the retina, upon which the light is focussed by the optical mechanism of the eye. Perfect vision, therefore, is dependent on the efficiency of the eye to act as a perfect optical instrument, and on the functional continuity of the nervous paths along which the stimulus must travel from the receptor station, the retina, to the perceiving station, the cerebral cortex.

In regarding the eye as an optical instrument, we must consider its structure, and also any active function it may have by virtue of its being a living entity: wherein it differs from a purely mechanical optical instrument.

The common simile of comparing the eye to a photographic camera is a useful one, conveying as it does the idea of a box containing several different media through which the rays of light must pass before they reach the sensitive plate.

The path of a ray of light through the eye to the retina lies through several different media—cornea, aqueous humour, lens, and vitreous humour.

The cornea consists chiefly of a transparent, white fibrous tissue, the substantia propria, containing a number of flat, plate-like cells (the corneal corpuscles). These are so arranged that their narrow diameter is at right angles to the entering ray of light, thus diminishing the amount of tissue through which the light has to pass. The cornea is covered on its outer surface by stratified epithelium situated on a homogeneous membrane (Bowman's Membrane). This corneal epithelium is in direct continuity with that of the conjunctiva, and is indeed a modification of it. It is therefore affected by similar pathological conditions as the conjunctiva.

The substantia propria, likewise, is continuous with, and a modification of the sclera, so that again we find that similar pathological conditions affect both.

The cornea is lined on its surface by a second homogeneous membrane (Descemet's Membrane), and covered by a layer of cubical cells. This membrane is very resistant to ulceration, and often prevents perforation.

Unless the substance of the cornea is clear, its surface smooth and curvature regular, there is an interference with vision. The cornea has no blood-vessels, and is simply nourished by lymph, although when ulcerated or injured, it becomes vascularized. Corneal ulcers, interstitial keratitis (non-ulcerative), and injuries bring about diminution of vision in this way, which may be temporary or permanent.

All corneal ulcers, which have penetrated Bowman's membrane and involved the substantia propria, leave a certain amount of scarring since repair is by fibrous tissue, which takes the form of nebulæ (white opaque patches) on the cornea. When very dense (leucomata) they may cause total blindness, and it is evident that a faint diffuse nebula covering the pupillary area causes more interference with vision than a denser one situated peripherally. Some forms of interstitial keratitis may clear up entirely, or may leave diffuse opacities all through the corneal substance, or, as in cyclitis (inflammation of the ciliary body), where numbers of small spots consisting of groups of cells on the back of the cornea (keratitis punctata) are often the only sign that a cyclitis is present, they may be sufficient to bring about diminished vision.

Alteration of the normal curvature of the cornea will also interfere with vision, as in astigmatism and conical cornea. The cornea, instead of being regularly curved like a portion of the surface of a sphere, is pointed and cone-like, and is not remediable by glasses.

In astigmatism, the curvature of the cornea is different in two meridia, which are usually at right angles to each other, e.g. horizontal and vertical, but suitable cylindrical lenses remedy this defect.

Conditions which affect the sclerotic or outer coat of the eyeball only interfere with vision when they involve the cornea. The sclera consists of thick, white fibrous tissue and is subject to inflammation (scleritis) which, when involvement of the cornea (sclerokeratitis) also occurs, may leave permanent scarring.

The aqueous humour is secreted by the columnar cells of the ciliary body. It fills the anterior and posterior chambers of the eyes and drains away through the canals of Schlemm, situated at the so-called filtration angle of the anterior chamber.

Its refractive effect on the rays of light is usually included with the cornea, and only when it becomes "muddy" through the presence of exudated cells does it interfere with vision.

Intra-ocular Pressure.—Just as the blood within the blood-vessels exerts a certain pressure on their walls, called blood pressure, so the contents of the

eye exert pressure on its coats known as intra-ocular pressure. It can be tested by getting the patient to look down, and then palpating the eyeball through the eyelid with the tips of the two forefingers, as if testing for fluctuation in an abscess, or by a special instrument called a tonometer. The normal tension is 20-22 mm. of mercury. If the drainage of lymph from the anterior chamber is interfered with, e.g. by blockage from exudate, then the intra-ocular pressure rises, and the condition known as glaucoma is produced, which may lead to complete blindness, which results from the effect of the pressure on the retina and optic nerve fibres. Treatment consists in increasing the filtration from the anterior chamber by the local administration of a drug, such as eserine or pilocarpine, which affects the parasympathetic nerve endings, and by constricting the pupil opens out the filtration angle. A similar result is brought about by partial removal of the iris (iridectomy), but it is important to recognize the condition in its early stage before degeneration of the nervous elements has occurred.

The lens consists of a large number of clear epithelial cells modified to form fibres and continues to grow throughout life. As the young lens fibres are laid down on the outside, those in the centre become more and more compressed and form a dense nucleus. If an adult lens is cut with a knife, the soft cortex is easily peeled off, leaving the harder nucleus.

The lens is covered with a fibrous membrane, or capsule, which acts as a protective covering.

In old age the lens becomes harder and denser, its refractive index increases, causing senile myopia. In addition it may show opaque areas known as *cataracts*. These may be in sectors, often worse at the periphery, or the opacities may be central or nuclear. In any case, the entire lens ultimately becomes opaque, and renders vision useless.

In some children in whom there are other signs of interference with development, the lenses may be congenitally opaque. If for any reason—usually following a perforating wound—the protective capsule is torn, the aqueous humour gains access to the lens substance, the fibres swell, and become opaque and the traumatic form of cataract is produced. The interference with vision in cataract varies with the amount of opacity, and in the case of the traumatic form, with the nature of the injury.

The vitreous humour consists of fibrous membranes arranged concentrically, and separated from one another by wide spaces filled with lymph. It occupies about four-fifths of the eyeball, but plays only a small part in refraction. It only interferes with vision when filled with opacities which may be

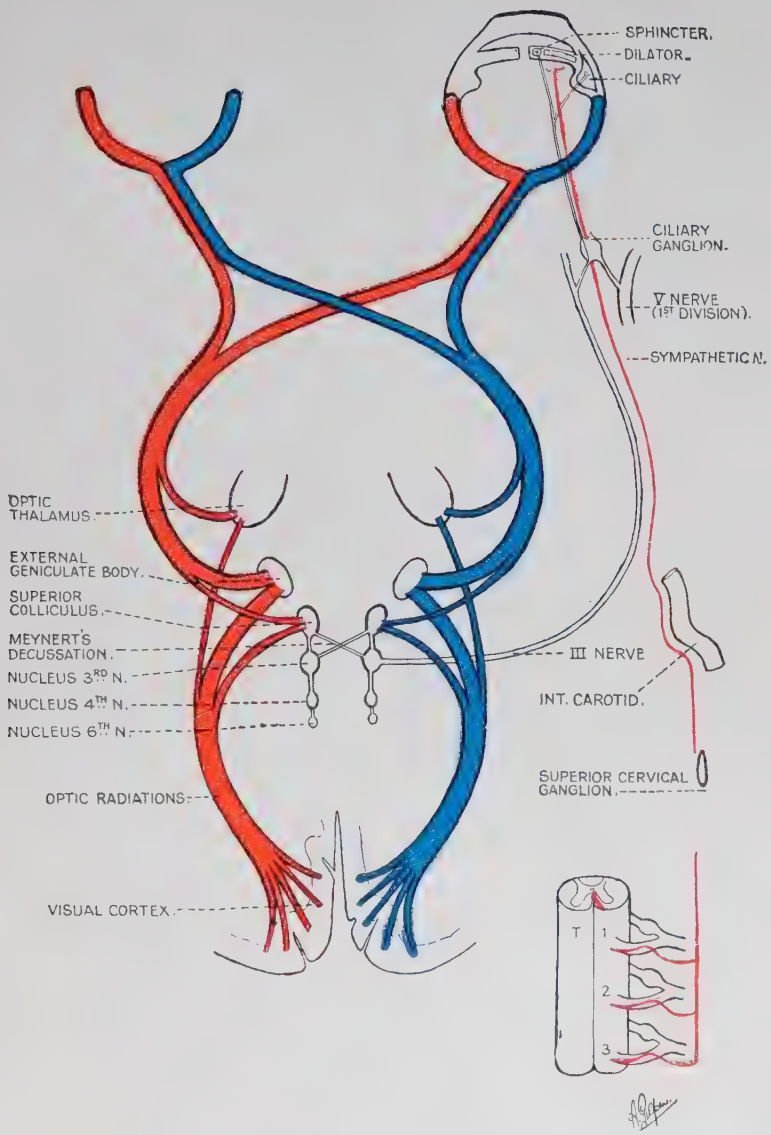


PLATE III. The Nerve Paths Related to Sight.

derived from the cells of the ciliary body, or from a blood clot due to a retinal hæmorrhage.

Refraction.—When a parallel beam of light enters a normal or emmetropic eye, it is so refracted by the media through which it passes that it is brought to a focus on the retina, with the result that the individual is able to see clearly the object looked at. Light rays proceeding from a distance greater than six metres are parallel, while if the object is nearer than this distance the rays are divergent. Such divergent rays will not come to a focus on the retina if the normal eye is in the resting position. In order that such rays may be focussed the lens becomes stronger or more refractile by increasing its curvature. Situated behind the iris and deep to the corneo-sclerotic junction is the fringe-like ciliary body with its ciliary muscle. It is the muscle of accommodation and is divided into two parts. One is a circular portion situated more internally and when it contracts it diminishes the transverse diameter of the eye. The other is a radiating portion arising from the above junction and passing back into the choroid. By its contraction it pulls the choroid and ciliary processes forward. The suspensory ligament becomes slackened, and the lens thickens owing to its elasticity. This increases its strength, so that it can now focus divergent rays on the retina. In old age this mechanism tends to fail, a condition known as *presbyopia*. It may be assisted by a suitable convex lens.

Abnormal focussing, or errors of refraction, occur when the eyeball is too short antero-posteriorly (hypermetropia), or too long (myopia). That refractive error due to abnormal curvature of the cornea is known as astigmatism.

In *hypermetropia* the lens fails to focus parallel rays, so that the image is a blurred one. Such an eye, however, can focus a convergent beam. This does not occur in nature, but may easily be made by the use of a biconvex lens, which therefore is the sort used in its correction. The eye itself tries to get out of the difficulty by an excessive amount of accommodation, with the result that it is never at rest. Moreover, when still further accommodation is required for near work, the supply is already used up. This gives rise to headache and eye strain from the excessive muscular strain.

In high degrees of refractive error, the two eyes do not work together comfortably, with the result that one is thrown out of action. This unused eye squints—in hypermetropia usually inwards (convergent squint) and in myopia outwards (divergent squint). A squinting eye never has good vision, owing to disuse. An eye blind from any cause always diverges.

In *myopia* the eye finds a partial means of overcoming the difficulty, by a contraction of the eyelids—hence the name myopia. This has the effect of

cutting out the peripheral rays, which have a shorter focal length, and only using the central ones, since they have a longer focus. The image is thus made a little clearer but, of course, is often then quite indistinct. A myope can focus divergent rays, and since parallel rays may be made divergent by a concave lens, this type is used in its correction.

In *astigmatism* the cornea is unequally curved in its horizontal and vertical meridians. It follows that the rays which come from one diameter of an object may be focussed on the retina, while those which come from some other diameter will be focussed in front of or behind the retina. This gives rise to blurring of the object, and can be corrected by wearing suitable cylindrical lenses, which are plane in the normal diameter and curved in the abnormal.

Only one example has been given, but all sorts of combinations exist and moreover the two meridia may be at any angle, though in regular astigmatism they are always at right angles to each other. Irregular astigmatism occurs when the cornea has been scarred by an injury or ulcer.

As we have said, sight originates in the stimulation of the retinal rods and cones, which are but nerve endings specialized for the perception of light. The cones are situated in the more central areas of the retina, and are concerned with accurate vision in a good light, the rods are responsible for vision under conditions of poor light. From these endings afferent impulses pass by way of a chain of two neurones to the ganglionic layer of the retina, whence arise fibres, which when collected together form the optic nerve. At the actual point where the optic nerve leaves the eye at the back and slightly to the inner side there are no nerve endings, hence it is called the blind spot, although in medical work it is more commonly known as the optic disc.

By the use of the ophthalmoscope, the retina is seen to present several distinct features of importance. Its red colour is the result of its blood supply, but should any area be destroyed it is at once evident by its pallor. A general pallor may result from the occlusion of the central artery, by an embolus or merely from spasm, a rare condition found occasionally in conditions such as migraine and quinine poisoning. This fact is, however, of some physiological interest as some hold that the symptoms of epilepsy are due to a similar spasm of the cerebral arteries, and that in this condition there may also be retinal spasm.

The retina is also nourished by the capillaries of the choroid, the pigmented layer lying immediately outside the retina, and supplied by the ciliary arteries. Any disease which affects the choroid therefore affects the retina also. Should the retina become detached from the choroid, the area separated becomes markedly paler than the rest of the fundus, and similarly in various forms of retinitis

and choroiditis pale areas due to the sclera showing through the atrophied choroid may be seen.

On the other hand, dark areas may appear on the retina usually caused by hæmorrhages, which are found in various forms of retinitis and general diseases, such as the anæmias, nephritis, or diabetes.

The disc is of special interest as it is normally a clearly defined area, easily seen, and often affected in disease. As it is the point of emergence of nerve fibres forming the optic nerve, and as its fibres are nourished from the ganglionic cells of the retina, little blood supply is necessary, and the disc looks appreciably paler than the fundus and may often be yellowish in colour. The colour of the disc may, however, approach that of the fundus in inflammation in the region of the retina, or in venous congestion. Such hyperæmia may be looked upon as normal where there are errors in refraction but may indicate the beginning of an optic atrophy. In this condition the smallness of the arteries with a striking pallor of the disc is evident, but it must be remembered that in many normal individuals the very centre of the disc is funnel-shaped and at its edges reflected light appears very pale.

The vessels of the retina stand out in contrast to the pale disc, from the centre of which is seen to emerge the central artery and the corresponding veins. The artery is distinguished by its comparative narrowness, and by the fact that it and its branches reflect more light from their surfaces. This reflection becomes especially well marked in arterio-sclerosis, when the arteries may also be tortuous and present a beaded appearance. An increase in the size of the veins, on the other hand, with distinct tortuosity, is to be taken, with other signs, as evidence of optic neuritis.

The veins may be seen to pulsate normally, but pulsation of the arteries is pathological and may be seen in glaucoma or aortic regurgitation.

The depth of the optic disc can only be appreciated by practice, but with glaucoma there is a distinct cupping, while the vessels are seen to bend sharply at the edge of the cup. If this condition progresses the signs of optic atrophy gradually appear.

The edge of the disc should be clearly defined, but in disease, such as a neuro-retinitis or papillitis (i.e. choked disc, in which the latter is swollen), this is no longer the case. Such optic neuritis is seen in a large variety of conditions, and it is of specially diagnostic significance in cerebral tumour.

The actual disturbance of vision which may result from various diseases of the retina and optic nerve, varies from slight loss of visual acuity to complete blindness. The sudden onset may be of value in diagnosis, as in retinal detach-

ment or occlusion of the central artery, but more commonly the onset is gradual, especially so when it is associated with general states of disease. Occasionally the disturbance in vision may lead to the causal disease being suspected. It will be clear, that the more the posterior pole of the eye is affected, the more likely is vision to be affected, especially if the lesion is in the macula lutea, which is that retinal area in line with the optic axis, where vision is most acute. In scotoma, due to tobacco poisoning, presumably as a result of some selective action, evening vision is better than that in a good light.

Lesion of the fundus generally, on the other hand, may not be appreciated at all. Various scotomata may be present without the patient's knowledge, and of course we are all unaware of the normal blind spot. It is possible as in squint, or in microscopic work, to disregard entirely what we see with one eye.

The field of vision can only be satisfactorily mapped out by the use of the perimeter, a cheap and simple apparatus. In this way may be shown the typical paracentral scotoma of tobacco amblyopia (commonly for red and green); the concentric contraction in tabes; and the typical diminution of the nasal side of the field in glaucoma. This instrument gives very important warning as to the necessity for treatment, which may be begun while there is yet time to save vision.

The paths by which the impulses reach the cerebral cortex are readily seen from Plate III. The fibres from the same side of each eye join together, crossing at the optic chiasma. For example, on the right side, the brain receives impulses from the left side of each eye. The optic tract is seen to pass to the primary optic ganglia, especially the external geniculate ganglia (although there is some discussion as to the exact connections in this region), and thence to the occipital lobe of the cerebral cortex in the region of the calcarine fissure.

The effect on vision of any lesion of this path will depend on the exact part of the tract affected. A lesion affecting the optic nerve will cause blindness in one eye, one in the region of the chiasma blindness on the internal side of each eye, while a lesion of the optic tract to the cortex will cause loss of vision in the opposite side of each eye. In each instance it will be evident that the field of vision will be deficient in the side opposite the actual eye blindness. The association of the occipital lobe with the perception of light is experienced by the flashes of light which are seen if a blow is received on the occiput.

THE REFLEXES OF THE EYE

The infinite variety of reflexes in the region of the eye is not only of physiological interest, but not infrequently of valuable diagnostic significance. Plate

III gives a comprehensive diagram of the pathways concerned. The retina is supplied by the optic nerve, and has been dealt with above. The chief motor nerve to the ocular muscles is the third or ocular motor nerve, which supplies all these muscles, except the superior oblique and external rectus, which are supplied by the fourth and sixth nerves respectively. The third nerve is also responsible for the innervation of the levatores palpebræ superiores, and with it also pass the parasympathetic fibres, which supply the sphincter of the iris and the ciliary muscle.

Interference with the path of the third nerve from its origin to its distribution will bring about an external squint as the result of the unopposed action of the external rectus with inability to move the eye inwards or upwards. If there is a lesion of the sixth nerve, the opposite condition exists, the patient having an internal squint with inability to move the eye outwards. Lesions of the third nerve are usually associated with changes in the pupil from paralysis of the parasympathetic fibres, and the power of accommodation is lost. The various positions and movements of the eye in conditions affecting the nerve tracts supplying its muscles make a most fascinating problem, which is, however, outside the scope of this book. Individual paralysis of such nerves seldom occurs as an isolated sign of disease. All the functions of the third nerve need not, however, be affected at once. Ptosis, for example, may exist, as in tabes, without there being any other evidence of oculo-motor deficiency. Where the lesion is cortical or between the motor area and the nucleus, there may be no interference with the parasympathetic fibres. In tabes the ptosis may be looked upon as being due to the paralysis of such fibres, which supply the upper lid.

The Conjunctival Reflex.—This reflex is designed to protect the cornea from injury and has for its afferent path the fifth nerve and its endings in the conjunctiva. When this path is stimulated the impulse passes backwards to the Gasserian ganglion, and thence to the oculo-motor nerve which brings about closure of the eyelid. If the stimulation is sufficiently severe, the nucleus of the seventh nerve is also stimulated, producing constriction of the orbicularis palpebrarum.

Reflex stimulation also occurs if a blow is seen coming towards the eye, but in this instance the path must depend on association fibres between the optic tract to which the optic nerve carries impulses and the nuclei of the third and seventh nerves. In paralysis of the latter, the reflex is limited to the eyelids of the diseased side. Even when the eye is closed, as the closure is unsupported by the orbicularis palpebrarum, it is found that it can be opened more easily than that of the other side by pulling up the eyelids. Inability to close the eye-

lids without tremor is seen in conditions of general nervous states, especially neurasthenia.

Absence of the conjunctival reflex is a convenient sign in determination of the depth of anæsthesia. At this stage the anæsthesia is sufficient for operation. Beginners have, however, to be reminded that too frequent stimulation of the cornea will cause the latter to become insensitive and on no account must a finger wet with an anæsthetic be used. Absence of the conjunctival reflex is occasionally obtained in hysteria and is associated with palatal anæsthesia. More commonly, however, it is retained and its retention is of value in the differentiation of hysterical and simulated fits from those due to more serious causes, such as epilepsy.

The Light Reflex.—By the light reflex the retina is protected from an excessive or dangerous amount of light. It is a true reflex, the afferent path being the optic nerve and tract to the corpora quadrigemina and thence by Meynert's fibres to the nucleus of the nerve (see Plate III). It seems likely, from the action of atropine, that the fibres of the third nerve which supply the iris sphincter are really parasympathetic in nature, although they have their origin in close association with the nucleus of the third nerve in the floor of the Aqueduct of Sylvius. Atropine is known to paralyse all parasympathetic nerve endings.

It is important to remember the bilateral nature of the stimulus, in any attempt to elicit the reflex. The stimulus for each pupil arises from half the retina of both sides. To obtain the reaction, both eyes must be shaded and one suddenly uncovered, when, if the patient has been asked to look towards the light, the pupil is seen to contract. Advantage is taken of this dual nature of the stimulus in Wernicke's method of investigating the optic tract. Thus if light is shone from a mirror upon one half of the retina only, the reflex will not occur if the lesion is between the optic chiasma and the corpora quadrigemina of the opposite side. If it is behind the corpora the reflex is unaffected, while if the optic nerve is affected the reaction cannot be obtained by stimulation of the eye on the same side.

In tabes, and general paralysis, the absence of the light reflex with retention of the reaction to accommodation—the so-called Argyll-Robertson pupil—is often obtained. It will be seen from Plate III that such a condition can be brought about by degeneration of Meynert's fibres which cuts off the efferent from the afferent neurone in the light reflex. It is clear from the figure that it is necessary to keep the eye not under investigation covered, for the third nerve nucleus may be influenced by stimuli reaching it from both eyes.

Normally the parasympathetic keeps up a reflex tonic action upon the pupil. This tone varies with the amount of light allowed to fall on the retina. It may readily be manifested by the fact that the administration of atropine which paralyses all sympathetic nerve endings, causes dilation of the pupil. Indeed, this action of atropine is responsible for the naming of the plant "belladonna," from which the drug is derived. It is used when it is desired to paralyse the sphincter in order to keep it out of a corneal wound, or to inspect the interior of the eye carefully. It is important to remember that by this atropine dilatation the mechanism of the reaction to accommodation is paralysed. On the other hand, the use of pilocarpine or of eserine which stimulate parasympathetic nerve endings brings about constriction of the pupil. We therefore use these drugs in the treatment of glaucoma where it is necessary to increase the withdrawal of fluid in the filtration angle.

The pupil is also innervated by the sympathetic, which maintains the tone and size of the pupil. There is a balanced action between this tone and that kept up by the parasympathetic accompanying the third nerve. Whenever there is dilation or constriction of the pupil there must also be reciprocal action between the parasympathetic and sympathetic nerves. The tone of the sympathetic is seen by the fact that if it is paralysed by section of any part of its pathway, or by paralysis of its nerve endings by ergotoxine, there is marked constriction of the pupil. The dilation of the pupil and of the blood-vessels on stimulation of the cervical sympathetic was, together with the effect of section noted above, first shown by Claude Bernard. Clinically, paralysis of the sympathetic may occur from a lesion anywhere on its long path. Preganglionic fibres for the supply of the eye pass out by the upper thoracic routes to the stellate ganglia, and thence to the inferior cervical ganglion, and in doing so form a loop round the subclavian artery known as the ansa subclavii. They then pass up the neck in the carotid sheath to the superior cervical ganglion, from which they are distributed along the internal carotid artery to the Gasserian ganglion. From this point distribution is with the nasal division of the fifth nerve, and finally by its branches, the long ciliary nerves. Some sympathetic fibres instead of taking this route pass from the vessels to the cavernous plexus and on to the ciliary ganglion. They are distributed like those of the parasympathetic, by short ciliary nerves. (See Plate III.)

Lesion of the sympathetic may be the result of a diverse number of conditions which may affect it throughout its course. Further, the lesion may be irritative or paralytic, which will bring about dilatation or constriction of the pupil respectively. Irritation or paralysis may, for example, occur where a

cervical rib presses upon the roots at their emergence from the spinal cord, or an aneurysm may press on the nerve in its later passage through the neck. An inequality of the pupils in such conditions often gives the key to the diagnosis. A slight degree of inequality of the pupils may, however, occur in conjunction with errors of refraction.

It is possible to stimulate the sympathetic by pinching the skin of the neck. The afferent path of this so-called cilio-spinal reflex is apparently by way of a sensory nerve, but where exactly the impulse becomes efferent is uncertain. The presence of the reflex is said to be an aid in the diagnosis of alcoholic coma. In actual fact any sensory stimulation brings about dilatation of the pupil just as it causes a rise of blood pressure and an increased rate of the heart, from sympathetic stimulation. As would be expected, dilatation is also produced by adrenaline. This does not occur normally, but only when the sympathetic has been previously destroyed. It also occurs in diabetes, in which it forms the basis of Loewi's test.

Where there is any excessive general sympathetic tone or diminished vagal tone we find dilatation of the pupil accompanying the increased heart rate and rise of blood pressure due to similar causes. Thus these signs appear in atropine or alcohol poisoning, in exercise, or in fright. A loss of vagus tone is seen too in deep anæsthesia, in cerebral compression causing cerebral anæmia, and at the point of death. On the other hand, constricted pupils due to the opposite cause are characteristic of cocaine and opium poisoning and hæmorrhage into the pons. In opium poisoning the marked constriction of the pupil, together with the smell of the breath, may be an important diagnostic aid. Constriction of the pupil is also seen in the first stage of chloroform anæsthesia, during which the parasympathetic tone of the heart is increased and cardiac stoppage is liable to occur. Later on the pupil becomes of medium size and immobile to light, at a stage before the conjunctival reflex occurs. In many operations an anæsthesia in which the pupillary reflex has disappeared and the corneal reflex is still present is of sufficient depth. Dilatation of the pupil under anæsthesia is an indication of impending disaster, commonly from respiratory or circulatory failure, and is marked at the point of death.

The **reaction to accommodation**, although strictly speaking not a reflex, is commonly investigated with the reflexes of the eye. Plate III shows that it is really a motor movement associated with convergence, and designed to cut off those parts of the field of vision less accurately focussed. More detailed images are produced by focussing on the macula which is straight behind the centre of the pupil. As the mechanism of accommodation is so closely related to that of refraction, it has been considered in relation to "Sight."

CHAPTER X

HEARING

By V. E. NEGUS, Ch.M., F.R.C.S., Assistant-Surgeon King's College Hospital, lately Hunterian Professor, Royal College of Surgeons.

General Considerations

The organ of hearing consists of two main divisions, if it is considered from the clinical aspect. The first is the *Conducting Mechanism,* which consists of the external and middle division of the ear; it is designed to collect and convey sounds from the external atmosphere to the sensitive endings of the auditory nerve. This division of the mechanism takes no part in the perception of sound, nor is it absolutely necessary, for even after its destruction hearing is in many cases fairly good, although diminished in acuity to a variable degree below the normal.

The *Perceiving Mechanism* is supplied by the cochlea; this is a coiled tube situated in the internal ear, where it is in communication with an organ of orientation, made up of the semicircular canals and the otolith systems of the utricle and saccule.

In the cochlea the effect of sound waves causes stimulation of the endings of the auditory nerve, by the fibres of which impulses are carried up to the brain, where they are analysed and appreciated.

The various parts of the conducting and perceiving apparatus will be considered separately.

EXTERNAL EAR

The external ear consists of two divisions; the *auricle* is the name of that part of the ear which projects from the side of the head, with the object of collecting sound waves. In many animals it has an important function; in man it is of but little use. It is to be noticed, however, that although its removal causes almost no change in acuity of hearing in the case of the otherwise normal individual, yet in the case of the deaf it must be of advantage. Indeed they reinforce it with the hand or an artificial device.

The *External Auditory Meatus* is a canal leading from the auricle to the middle ear; it is separated from the latter by the tympanic membrane, on which

sound waves impinge after travelling in from the exterior. The canal is protected near the surface by a sieve-like arrangement of hairs; in conjunction with sticky cerumen secreted by specialized glands lying in the cartilaginous portion of the tube, they give protection against the entrance of insects and dust.

Any marked interference with the patency of the canal causes deafness, because sound waves are prevented from reaching the tympanic membrane, but the canal may be reduced to very narrow limits, short of being completely occluded, without loss of hearing.

The factors likely to obstruct the canal are large collections of cerumen mixed with dust and soot, swelling of the epidermal lining caused by a boil or furuncle, and the presence of a foreign body such as a pea.

MIDDLE EAR

The middle ear consists of Eustachian tube, tympanic cavity, tympanic membrane, mastoid antrum and mastoid air cells; it is with the three first mentioned structures that we are particularly concerned.

The *Eustachian Tube* brings the nasal fossa into communication with the tympanic cavity; it is only occasionally open, however. It is of importance in that it serves to regulate the air pressure in the middle ear tract, and if it is obstructed serious impairment of hearing may be the result.

Such obstruction is caused by inflammatory swelling associated with rhinitis, or to blockage by adenoid tissue or a naso-pharyngeal neoplasm.

After occlusion of the tube, air contained in the tympanic cavity is absorbed to a certain degree, and the pressure falls below that of the atmosphere. The result is that the tympanic membrane is drawn inwards, and presumably the membranes closing the round and oval windows of the inner ear must be drawn outwards. Transmission of sound from the external auditory meatus to the cochlear mechanism is interfered with and deafness is produced.

Violent blowing of the nose may force air through the obstructed Eustachian tube and cause a sensation of bulging of the tympanic membranes. A similar result may be brought about by swallowing with the mouth and nose closed, in which case the raising of the soft palate causes at first an increase of pressure in the nasal fossa, and consequently of that in the tympanic cavity also.

Forced expiration with the nostrils closed brings about the same result, and is a method often adopted by those with obstructed Eustachian tubes; frequently repeated bulging of the tympanic membrane may, however, cause stretching of its tissues, with deleterious results. A more accurate method of inflation of

the middle ear is that in which air is blown into one or other nostril from a Politzer bag. In severe cases the Eustachian catheter is used.

It is probable that in many cases it is not obstruction, but undue patency of the Eustachian tube which is the cause of deafness.

The *Tympanic Membrane* shuts off the middle ear from the external meatus. It has a central fibrous layer covered with epidermis and mucous membrane.

It can vibrate through a very wide range of pitch and is practically dead beat, without after vibrations.

The *Tympanic Cavity* is bounded partly by bony walls, and partly by the membranous tympanic membrane and the membranes of the round and oval windows; in it lie the tympanic ossicles. Sound can be conducted across the cavity without the assistance of the chain of bones, as is found to happen in many individuals who have had middle ear disease; very often a fair degree of hearing is retained in spite of severe damage.

The *Ossicles* are so arranged that they link the tympanic membrane to the membrane of the oval window. There is a slipping joint between the malleus and incus, so designed that excessive movement of the stapes shall be prevented, as otherwise there would be a danger of rupture of the membrane filling the foramen ovale.

The area of the tympanic membrane is much larger than that of the oval window, so that sound waves coming from the exterior are concentrated to a considerable degree. At the same time the lever action of the ossicles is one which diminishes the amplitude of the sound wave and greatly increases their intensity.

Middle Ear Deafness results from any condition which interferes with passage of sound waves from the exterior to the windows of the labyrinth.

Under this heading are included cases of deafness due to obstruction of the external auditory meatus; the signs and symptoms are identical, whether the obstruction is situated in the external or middle ear.

Other conditions producing middle ear deafness are inflammatory changes or perforation of the tympanic membrane, indrawing of the membrane by diminished pressure in the middle ear tract, arthritis or ankylosis of the ossicles, dislocation or destruction of parts of the malleus or incus, exudation of serous or purulent fluid into the tympanic cavity, and the obstruction of cholesteatomatous collections or granulation tissue.

In the normal individual sound is heard more clearly when it passes through the auditory meatus than when it is conducted through the temporal bone. Thus, if a vibrating tuning-fork be held to the skull behind the ear until its

sound is no longer heard, it will again be perceived if held close to the orifice of the auditory meatus, the reason being that the waves entering the meatus are collected and amplified by the tympanic membrane and ossicles.

In cases of middle ear deafness this relation is upset; the obstruction to passage of sound waves through the conducting mechanism causes a tuning-fork or other sound-producing apparatus to be perceived better when pressed against the bone than when held close to the auditory meatus. This is known as *Rinné's test* which is called positive in the normal individual and negative in those with middle ear deafness.

Not only is sound heard better when conducted through bone than when heard through the air in cases of middle ear deafness, but furthermore a tuning-fork held on the middle line of the skull in such a case is heard best in the unhealthy ear. This is known as *Weber's test;* and may be readily imitated by blocking the auditory canal with the finger. It has been suggested that the fact why the tuning-fork is heard better in the impaired ear is due to the absence of confusion by external sounds, and this is supported by the fact observed by Jenkins that under conditions of extreme quietness closure of the auditory canal does not result in better hearing of a tuning-fork in the closed ear. This observation is still further supported by the observation (McDowall) that if both auditory canals are blocked up by the fingers, the breathing sounds can be heard, although they are normally inaudible.

The *Action of the Tensor Tympani Muscle* has been studied for many years and especially in recent years by workers at Utrecht. The muscle is situated in a bony canal lying alongside the Eustachian tube, and is inserted into the handle of the malleus. It may be observed to contract in response to any sound, and it was supposed at one time to render hearing more acute. As it contracts to low tones as well as to high, the explanation does not seem to be satisfactory, but none other can be put forward. Contraction is said to be greater when high tones are sounded. The tympanic membrane is drawn inwards by the muscle, and condensation of air in the tympanic cavity produced by its contraction appears to lead to increased pressure on the membranes of the round and oval window, thus raising intra-labyrintheric pressure.

The *Function of the Stapedius Muscle* has not been determined. The muscle issues from a small opening in the Fallopian canal, and is inserted into the neck of the stapes. When it contracts it causes the ossicle to rock in the oval window about an axis which passes through the junction of the posterior and middle thirds. It appears to act as an antagonist of the tensor tympani in regulating intra-tympanic pressure. As is evident from the sensations of temporary deaf-

ness experienced when pressure in the tympanic cavity is suddenly raised or lowered, it is important that some mechanism should be present to control the movements of the ossicles when sound waves impinge on the membrana tympani and cause it to rarefy and condense the air column lying against its inner surface.

INTERNAL EAR

The internal ear is the receptor organ for sound waves, which normally reach it through the conducting mechanism of the external and middle ear. For details of its structure the reader is referred to a textbook of physiology.

For present purposes it may be considered as a spiral canal divided into three compartments. The upper contains perilymph and receives impression of sounds transmitted by the movements of the stapes in the oval window. The waves travel through a fine opening into the lowest compartment, which is closed at its basal extremity by the membrane of the round window. Although sound waves are probably transmitted in this way when the conducting apparatus is normal, yet it seems likely that in cases where disease has destroyed the membrana tympani and ossicles, sound waves travel in the opposite direction; it is known that under such conditions pressure changes act most effectively on the round window.

Between the upper and lower compartments of the cochlea there is a third canal filled with endolymph, and it is here that the actual reception of sound takes place.

This canal is triangular in section, one side being made up of the basilar membrane. This is composed of a series of transverse fibres loosely held together. Each fibre is stretched, and resonates in harmony, when sounds of pitch corresponding to its rate of vibration reach the ear and cause waves to travel along the upper compartment, through the narrow communication, and thence along the lower passage. The fibres are shorter, more tense, and of less mass at the base of the cochlea, and are longer, slacker, and more heavily loaded at the apex, according to reliable views. Sounds of high pitch bring about vibrations by resonance and consequent stimulation of the basal fibres, while those of low pitch affect the apical fibres.

The vibrations of the fibres are transmitted to hair cells, which form part of the organ of Corti, a structure lying on the basilar membrane. From the hair cells fibres of the auditory nerve conduct impulses to the brain.

Internal Ear Deafness.—*Pathological Changes in the Oval Window* occur in many cases of a familial disease known as otosclerosis. Limitation of movement or fixation of the stapes is produced, with a type of loss of hearing

showing most of the signs of middle ear deafness. The process may spread to the capsule of the cochlea, and will then give rise to signs of internal ear deafness. There is one peculiar feature in all cases of otosclerosis, namely, paracusis or the ability to hear better with the affected ear in a noisy than in a quiet place. It is thought to be due to abnormal inertia of the stapes caused by its limitation of movement. If sounds of powerful intensity are brought to bear, they will overcome this abnormal inertia of the stapes, and enable other sounds of feeble intensity to be transmitted to the cochlea.

Pathological Changes in the Canals of the Cochlea produce characteristic signs. The changes may be due to inflammation of simple or syphilitic nature, to effusions of blood, or to injury. Sounds—such as those of a tuning-fork—are heard better by air conduction through the external auditory meatus, than by bone conduction through the skull; Rinné's test is therefore positive. The reason is that in the former case the intensity of sound is greatly magnified by the agency of the tympanic membrane and chain of ossicles, if they be healthy.

Hearing may be partly or completely lost, and it is to sounds of high pitch that perception is first diminished, but why this should be so is by no means clear. Recent pathological findings appear to call for a reconsideration of the generally accepted reasons.

Since the sensitivity of the receptor apparatus is diminished, sounds conducted directly by bone are not perceived so well as in the normal individual. A comparison between the affected person and the normal observer is known as Schwabach's test.

Since the affected ear does not hear sounds so well by bone conduction, if, as in Weber's test, a tuning-fork is held on the mid-line of the skull it is heard better on the good side.

Pathological changes in localized regions of the cochlea have been observed in boilermaker's deafness, and the loss of hearing in these cases has been demonstrated by Ritchie Rodger to affect that part of the cochlea concerned in hearing the particular sounds among which the men work.

Senile Deafness is of the internal ear type; the fact that hearing of tones of high pitch is the first to be diminished may be due to the loss of elasticity which must be the fate of fibres of the basilar membrane in old age. This loss leads to diminished power of rapid resonant movement, and must affect most severely the fibres of most rapid rate of vibration, namely those responding to high tones.

The Nervous Paths from the basilar membrane to the brain consist of the

hair cells, the fibres of the auditory nerve, the nuclei in the pons, and the tracts up to the temporal lobe via the auditory radiation.

In going to the brain the nerve passes by other important structures, so it is possible to localize a lesion by associated signs.

Thus, lesions in the internal auditory meatus or along the course of the eighth nerve, are usually accompanied by changes in the vestibular or facial nerves. The most common cause of trouble in this situation is an auditory nerve tumour, of which the earliest signs are loss of hearing of tones of very low pitch. The lower tone limit is gradually raised, until in the end deafness becomes complete. Vestibular disturbances are associated with the deafness, and facial paralysis often appears as a late sign, together with signs of raised intracranial pressure such as headache, vomiting and optic neuritis. Lesions of the pons affect various ascending or descending tracts at the same time as the auditory nerve fibres, and the resulting signs will be of use in localization.

The common causes are tuberculous lesions, gummata, new growths, and various types of sclerosis. In some cases the cerebellum is involved, and various localizing signs are then apparent.

Lesions of the crura cerebri, or of the temporal lobe of the brain will give rise to certain disturbances, which can be used in an investigation of a case where the loss of hearing is suspected as being due to such a condition. Such cases are, however, of rare occurrence. (See "Aphasia.")

Tinnitus is the term used to describe noises heard in the ears without external cause.

It is probable that the sounds are produced by various normal processes in the body, such as the rushing of blood along arteries, or of air through the trachea.

If an observer listens through a stethoscope, of which the chest piece is attached to that of a second stethoscope, and if the ear pieces of the second instrument are placed in the ears of any individual, he will hear obvious sounds. The reason why the individual does not hear the sounds of his own body is because of purposive lack of attention, or a psychological ignoring of them. In those with deafness, especially of the type of otosclerosis or internal ear deafness, external sounds are less well heard, but those of internal origin become distinct, and in many cases give rise to great distress.

CHAPTER XI

THE RATE OF THE HEART

In considering here the rate of the heart it must be understood that the organ itself is in a normal state and all its chambers respond in a physiological sequence. Conditions under which different parts of the heart vary in rate are considered in a succeeding chapter.

The rate of the heart, although conveniently elicited by an examination of the pulse, is more accurately determined by auscultation. In most individuals it beats at a rate of 65 to 75 per minute, but it must be remembered that many normal people have a cardiac rate considerably more or less. In infancy, the rate is about 120, and this may be maintained for several years. Napoleon is credited with a pulse rate of from 40 to 50. The physician, then, must be wary before reaching a conclusive opinion as to the significance of the pulse rate in an individual case he has not seen before.

The rate is set by that part of the heart called by Erlanger, the pace-maker, which is synonymous anatomically with the sino-auricular node of Keith and Flack. It corresponds to the sinus venosus of the frog, and lies in the right auricle near the entrance of the great veins. The circulation is, however, but the servant of the body as originally emphasized by Broadbent and others of the old Edinburgh school and more recently by their pupils Haldane and Mackenzie. The rate of the heart as set by the pace-maker serves the body at rest, and were the rate fixed, body function would be extremely limited. The circulation is under both nervous and chemical control, and as we shall see also in relation to the respiratory system, is adjusted so that it can respond with extreme delicacy and rapidity to the varying requirements of the body. Whenever the muscles are used carbon dioxide is produced, and this in itself causes a demand for greater circulation. Carbon dioxide in moderate quantities brings about a local dilation of capillaries (as first shown by Severini), which assists not only in the elimination of the carbon dioxide itself, but in increasing the supply of oxygen and energy.

To understand how the rate of the heart increases the blood supply to the body in general, it is necessary to review the factors governing the output of the heart, regarding which a great deal of knowledge has come to us from the use of the heart-lung preparation of Knowlton and Starling.

The output of the heart may not necessarily be increased by a mere increase in rate, since as a result of the increase the organ has less time to fill, and the output per beat is appreciably reduced. By increasing the rate it is the diastole rather than the systole which is shortened. Similarly, within physiological limits, the resistance to the outflow of the heart may be appreciably increased without causing any diminution of outflow.

This will be of great advantage at the beginning of exercise when there is an appreciable rise in peripheral resistance and in blood pressure. This increase of blood pressure is brought about by the constriction of probably all blood-vessels, especially in those areas not affected at the commencement of exercise, such as the skin (McDowall) and alimentary canal.

The essential factor governing the output of the heart is the inflow, a fact which is called by Starling the Law of the Heart. This indicates that within physiological limits the force of the heart's contraction depends on the extent to which the heart muscle has been stretched by the blood—a law which really applies not only to the heart but to all muscular tissue. Normally, however, as pointed out by Yandell Henderson, and which can readily be demonstrated, the normal venous pressure is such that the heart can fill in less time than the normal diastole. Still more is it true when the venous pressure is increased, as in exercise. A reduction in diastole does not diminish the filling and the output per beat. Normally, there is not only an increase in the number of beats but also an increase in output per beat and per minute.

We shall now consider the various mechanisms by which an increase in the heart rate is brought about. The heart is governed by two sets of nerves from the autonomic nervous system:—the sympathetic, whose effect is accelerative, and the vagus, whose effect is inhibitory. The sympathetic fibres arise from the upper thoracic roots, and reach the heart by way of the inferior cervical ganglion, and also, according to some, the superior cervical ganglion. Normally there is a balance between these two, being slightly in favour of the vagus, whose tone is the stronger. This vagus tone is essentially of a protective nature, and its development depends greatly on the requirements of the individual. Thus, pet animals have appreciably less tone than more active field animals, as is seen by the effect of vagus section. Similarly, in old age in man, there is diminished vagus tone, as is seen by the fact that the effect of atropine (which paralyses the vagus and hastens the heart) becomes appreciably less (Crawford). An increase in the rate of the heart is produced by diminution in vagus tone, or an increase in sympathetic or both, and this occurs in exercise. It is brought about, as shown by Bainbridge, by a rise in venous pressure. This rise of pressure in

the large veins of the thorax, and in the right auricle, is caused by many factors. In the first instance, the carbon dioxide produced constricts the veins directly, and also by central action, for we know from the work of Donegan and others that the veins are supplied by vaso-motor nerves. Further, there is an increased blood flow to the thorax, owing to the increased respiratory movement which occurs at the same time (page 145), while the movements of the muscles themselves, in virtue of the valves in the veins of the limbs, hasten the return of the venous blood. Over-filling is prevented by the pericardium. The increased flow of venous blood to the heart would, from its direct effect on the heart, be sufficient by itself to increase the output—both per beat and per minute, without necessarily a change in rate. A further increase, however, is brought about by Bainbridge's reflex, which still further augments the output. The latter showed that the effect of the rise in venous pressure does not depend wholly on direct action on the heart, but that there is a diminution in the vagus and an increase in the sympathetic tone.

The exact significance of vagus tone appears to be to permit the production of a higher venous pressure without an undue increase of cardiac rate, thus conserving cardiac energy. It has been pointed out elsewhere by the writer that vagus tone or restraint is the necessary corollary of the Law of the Heart. Without such restraint it would not be possible for the heart to take full advantage of an increased efficiency since by the Bainbridge reflex its diastolic filling would tend to be reduced while the operation of the Law of the Heart depends on an increased filling per beat.

From the above it will be evident that for the most part the muscles, in virtue of the carbon dioxide they produce, control their own blood supply, although indirectly,—by means of the nervous mechanisms which control the heart and vaso-motor system.

The existence of a nervous mechanism to control the heart is to make its response more immediate, and this is facilitated by the existence of a balance between the vagus and sympathetic which may be directly altered by higher cerebral centres. The heart rate of a sprinter at the starting-post is already increased ere the race begins. The same may be said of the respiratory rate. By these means there is no lag and the heart is ready to deal with the effects of the anticipated exercise. It is really a primitive mechanism intended to prepare for an emergency, such as a fight or the seizure of food—the successful issue of which was an essential of primitive existence. Pain also increases the heart rate, as does stimulation of any sensory nerve, and these may be considered as part of the same mechanism. Even the examination of the patient by the

physician may be sufficient to cause an undue hastening of the heart. Hence the pulse rate should not be taken until the confidence of the patient has been obtained. Several other concomitants of exercise facilitate an increased cardiac rate. During exercise, the venous blood from the exercised part is noticeably hotter than normal, and heat stimulates the pace-maker. Hence in fever the rate of the heart may be increased by a variety of causes—the pain, the temperature of the blood, and the toxin responsible for the fever. The mechanism by which the toxin affects the heart rate is as follows: as soon as the heart is poisoned and fails to drive out its full contents, the venous pressure tends to rise. This is very efficient in increasing the rate by direct and reflex effect on the pace-maker. This will be still further supplemented by the reduction of the depressor impulses passing up from the aorta, and a consequent reduction in the vagus restraint. The output of the heart, although reduced per beat, is, in view of the increased rate, not reduced per minute and the blood pressure is maintained. The increased heart rate where it is not associated with any other symptoms such as fever or pain, is often most important clinically. For example, in appendicular abscess, when the acute symptoms have passed off, the temperature may have fallen and the pain disappeared and one may be tempted to imagine that the attack has subsided. The increased cardiac rate is then of primary diagnostic significance together with local signs. Obscure conditions, such as early tuberculosis, are often suspected as the result of a rapid pulse.

In pathological conditions not associated with toxæmia, but in which there is a breakdown of some part of the mechanism for the conveyance of oxygen or carbon dioxide from and to the lungs respectively, the increased cardiac rate indicates that the circulation is influenced thereby and is probably attempting to make up to some extent for the breakdown. The mechanism of the acceleration of the heart may vary slightly in individual cases, but usually the action is by means of a raised venous pressure affecting the pace-maker. This is well seen in chlorosis, in which the increased rate of the heart is often the most striking symptom. In this case the increased volume of blood, as found by Lorrain Smith, will lead to an increase in venous pressure and, indeed, the fact that the heart rate is increased may be taken as supporting the conception that in this condition there is dilution of the blood.

The well-known tendency to œdema of the lower extremities in chlorosis may be looked upon as due to this dilution together with the rise in venous pressure. A further factor which may also play a part in the production of excessive heart rate is the inefficiency of the blood as a carbon dioxide and lactic acid carrier. We know that the corpuscles indirectly affect considerably the

amount of carbon dioxide which can be carried by the plasma (see Appendix) without affecting the H ion concentration of the blood. As will be seen in relation to "Breathing," there will tend to be an accumulation of carbon dioxide in the medulla. This stimulates the vaso-motor centre, which is very sensitive to carbon dioxide, raises the venous pressure and so accelerates the heart. Possibly also small amounts of carbon dioxide may have a direct effect on the cardiac centres, although we know that larger amounts increase the vagus tone and slow the heart. Impairment of the heart, where there is circulatory delay, will be a further factor in increasing its rate. In heart cases also, the venous pressure may be raised by the same means as have been referred to above in relation to the effect of toxin, that is, the banking up of blood on the venous side may be largely responsible for the acceleration.

The enormously increased heart rate which is so important in exophthalmic goitre is most likely brought about in several ways. The excessive secretion of the thyroid has probably a direct hastening action upon the heart metabolism, as it has upon other tissues. This may be further increased by its general stimulating action on the side of the sympathetic. Since there is a markedly increased metabolism, there must be an increased carbon dioxide production which will act as in exercise. This explains why dyspnœa is also a common symptom.

The heart rate in relation to the thyroid (page 202) may be taken as a general indication of the state of the patient. Thus in exophthalmic goitre the heart rate is excessive, and in myxœdema extremely slow. In the latter the rate can be taken as an indication of the effect of treatment by thyroid. It is usually considered safe to give the extract in increasing doses so long as the rate does not exceed a hundred per minute.

The heart may also be stimulated by specific substances ingested, e.g. tea, coffee, and after the average meal there is a normal increase in the heart rate. The accelerating effect of alcohol in concentrated spirits, such as brandy, is considered due to the sensory stimulation of the mucous membranes, but there are undoubtedly other factors concerned.

Tachycardia, produced by excessive use of tobacco, depends, however, on the effect of the nicotine on the nerve supply of the heart. Nicotine, as shown by Langley, paralyses the synapses in the ganglia of the autonomic system. In the case of the heart both vagus and sympathetic ganglia are probably affected. Since the balance is on the vagus side, the result of the paralysis is an increase in the heart rate depending on the tone of the individual. Atropine and belladonna preparations, on the other hand, increase the rate by paralysis of the vagal

endings, and so removing the normal inhibitory mechanism. These facts besides being seen in man can also be readily demonstrated in animals.

Hence, in considering the rate of the heart, a large variety of factors are concerned. They are all comparatively straightforward to deal with, if the general mechanism of heart control is kept in mind. The study of individual cases in the light of modern knowledge offers an excellent field of clinical study.

It will be noticed that the mechanisms used in disease are those normally developed for exercise, a fact which goes to emphasize that exercise by keeping the normal vascular reflexes and heart efficient is of enormous benefit in a sudden emergency, normal or pathological.

One note of warning in relation to the significance of an increased heart rate is necessary. It is commonly assumed that drugs (e.g. amyl nitrite, alcohol) which accelerate the heart are cardiac stimulants, but this may often be a grave error. The heart may be accelerated reflexly in an attempt to maintain arterial pressure should conditions arise which would tend to lower it, e.g. diminished peripheral resistance or increased capacity of the circulation.

In general it should be realized that in an individual whose normal heart rate under definite conditions is known, an increase in the rate may be of very appreciable significance, as it may be the first indication of approaching cardiac enfeeblement or the effect of toxemia. According to Mathew, this is often seen in cases of high blood pressure in which the rate is, for reasons indicated on page 120, usually slow.

Bradycardia.—A very slow heart occurs in individuals who take a large amount of strenuous exercise, and is produced by training, presumably as a result of increased vagus tone (see page 323). When it occurs in other individuals it is commonly found that they have been the subjects of pathological states, e.g. pneumonia and painful conditions, which like exercise have previously caused an excessive rate. The subsequent bradycardia may be looked upon as a physiological overcompensation, the mechanism of which is incompletely understood, although there is evidence which suggests that it has a chemical basis.

Such bradycardia must be clearly distinguished from the slow heart which occurs in impairment of the auriculo-ventricular bundle (see "Heart-Block," page 98) or that of myxœdema.

CHAPTER XII

THE PULSE AND THE HEART SOUNDS

THE PULSE

The examination of the radial pulse has been made by physicians from the earliest times, and to-day it continues to be a clinical observation of the first importance. The significance of the pulse, however, has only been gradually understood. It has long been recognized that its character varied under different conditions, and the old physicians did what they could in its interpretation. This was done with more accuracy than perhaps is generally admitted, but, not fully understanding the factors on which it depended, they inevitably classed together many conditions which are really quite different. The main features of the pulse are its rate, rhythm, and character. These will now be considered separately.

The Rate of the Pulse.—Physiologically, the pulse rate indicates the rate of the heart, but this is not sufficiently accurate for pathological requirements, as in diseased conditions the beat of the heart itself may be broken up in diverse ways. The radial pulse rate essentially indicates the number of beats of the left ventricle of sufficient magnitude to cause a wave to be conducted out to, and felt at, the periphery. The most convenient vessel for palpation is the radial artery. This wave passes to the periphery just as a ripple reaches to the edge of a pond, when a stone is thrown into it. If the energy of the wave is too small it is not felt, and if the heart is beating irregularly it is often found by listening to the organ itself that the ventricle is beating more rapidly than the radial pulse would lead us to suppose. The most sensitive means of feeling the pulse is by the three middle fingers, for with these, waves may be appreciated which cannot be felt by the thumb.

Further, the rate of the left ventricle is not necessarily that of the whole heart, whose auricles may, in certain pathological conditions, be beating appreciably faster. The rate depends on two factors: (1) the number of impulses reaching the auriculo-ventricular node from the right auricle, and (2) the conductivity of the auriculo-ventricular bundle of His. Provided the heart is normal, the ventricle follows the auricle beat for beat, and, except when the bundle is inadequate, the auricular rate determines that of the pulse. Failure of the

bundle is, however, comparatively rare, and although in general the pulse may therefore be considered an indication of the whole heart, this is not always true. Commonly, then, that which affects the rate of the auricle, will affect that of the whole heart, and the pulse. These have already been fully dealt with in the previous chapter.

Several pathological conditions, however, vary the number of impulses which reach the auriculo-ventricular node from the auricle and affect both the rate and rhythm of the pulse (page 98).

The Conductivity of the Auriculo-ventricular Bundle.—We know that the cardiac impulse commences at the Keith-Flack node (or pace-maker) of the right auricle in the region of the entrance of the great veins. The impulse passes out over the auricle, fanwise according to Lewis, and reaches the auriculo-ventricular node. It passes from auricle to ventricle by a specialized tissue, known as the auriculo-ventricular bundle. This starts from the auriculo-ventricular node, and runs to the inter-ventricular septum near the aortic valve, where it divides into two branches, one for each ventricle. These run down the septal wall and are continued on to the papillary muscles and the Purkinje fibres, which lie immediately under the endocardium. The bundle is further specialized in that it permits the passage of the impulse at a great speed, 5,000 metres per second, as compared with 1,000 metres per second in the rest of the heart. In this way a minimum of time is lost in the distribution of the impulse to different parts of the ventricle.

The bundle is the only pathway by which impulses can pass from auricle to ventricle, and it is therefore essential that it should be intact. Experimentally, in mammals, it may be severed, while in the frog, by tying the first Stannius ligature between the sinus venosus and auricle, an analogous condition may be produced. In this latter case, however, it is the muscle which is interfered with, the muscle of the sinus being continuous with that of the auricle and ventricle. This is not so in the mammal. When the conducting path between sinus and ventricle is interfered with, the latter may stop altogether, as it usually does in the frog, or it may continue beating, depending on the tension inside the ventricle itself. It has been noted, for example, that the stoppage is more apt to occur when the first Stannius ligature is tied at the end of systole, the heart being then empty. The tying of the so-called second Stannius ligature (around the auriculo-ventricular junction) by increasing the tension in the ventricle, usually restarts the latter, if it has stopped, though in the frog the new rate is much less than the normal. An analogous condition may be seen in the mammal, where the tension is kept up by the blood within the ventricle and

coronary arteries. If the auriculo-ventricular bundle is severed, the auricle continues to beat at its normal rate, but the ventricle takes on a much slower rhythm. Such a condition is known as *heart-block,* and clinically is met with in pathological states such as gumma, in the region of the bundle. It may also be induced by the undue use of cardiac tonics, which depress the conductivity of the bundle, and by a large variety of infective conditions, where it may be taken as an indication that the general myocardium has been impaired.

Recognition of heart-block obviously depends on the slow beat of the ventricles (and the consequent slow pulse, which must not be mistaken for a simple bradycardia), and the finding of a normal rate in the auricle. This may be evident from the pulsation in the great veins of the neck when the patient is lying down, from an examination by means of the polygraph, or the electro-cardiograph. Moreover, there is usually an enormous pulse pressure, for the systolic pressure may be high, and the diastolic very low. Varying degrees of heart-block have been found to occur. There may, indeed, be only a simple delay in the conduction of the impulse to the bundle, which is only detected by the polygraph, and electro-cardiograph. Here there may be an undue length of the *a–c,* or P–R intervals respectively. Again, there may be only an occasional failure to conduct, giving the appearance of missed beats. This rare variety will have to be differentiated from the condition of extra systole, which is dealt with below.

The Rhythm of the Pulse.—The impulses initiated by the pace-maker are sent out at a regular rhythm, the interval between each pulse beat being constant, usually, in man, at about 0.7 or 0.8 per second. Normally the left ventricle beats similarly, and the pulse at the wrist and elsewhere is appreciably regular. When, however, the ventricle does not receive its stimulus regularly, then the pulse must necessarily be irregular. This we have noted as a possible result of intermittent heart-block.

More commonly, the pulse is irregular, because the auricle does not pass on impulses at a regular rate, either because the auricular muscle does not contract uniformly, or because abnormal stimuli originate in the auricle. It is possible that the pace-maker may be slightly irregular in its action, as is evident in the condition of sinus arrhythmia, so-called because the node corresponds to the primitive sinus of the lower animals.

Sinus Arrhythmia.—This is merely an exaggeration of the normal effect of respiration on the heart. It rarely produces symptoms, or is a serious condition, although its existence has to be appreciated. At each inspiration the negative pressure in the chest is increased, blood is drawn into the thorax, and the

descent of the diaphragm drives blood from the abdominal veins upwards. This has been described by Leonard Hill as the "respiratory pump." The increased filling of the auricle which results, causes a diminution in the vagal, and an increase in the sympathetic tone, as shown by Bainbridge, and an increase in the rate of the heart. At the same time there is diminished pressure in the pericardium, as pointed out by Lewis, and this still further tends to increase the rate. For the sake of completeness it may be remarked that, as emphasized by Sharpey-Schafer, there is diminished resistance in the pulmonary circuit. All these factors together tend to produce an increased cardiac output during inspiration, and a rise of arterial pressure. It has also been shown by Bainbridge that the hastening of the heart from increased original filling, depends on the integrity of the nervous connections which can be partly thrown out of action by atropine, which paralyses the vagal endings. Hence we find that sinus arrhythmia is usually abolished by the administration of this drug, which is a useful aid in the differential diagnosis of the condition. It is not, however, an absolute test, for it does not affect the pericardial or sympathetic factors.

Another condition in which the pulse is irregular is that of Extra Systole.

Extra Systole.—By this is meant a premature contraction of the ventricle, not dependent on an impulse from the pace-maker, but originating from an abnormal stimulus within the auricle or ventricle itself. This contraction may be quite small, as the heart may scarcely have recovered from previous contractions, and the pulse wave produced may be too small to be appreciated at the wrist, although the extra beat may be detected on auscultation of the heart itself. It may also be felt by the patient himself, as a fluttering sensation in the cardiac region, but more often it produces no symptoms. The irregularity usually disappears after exercise. An analogous condition can be readily produced experimentally. If, when the heart of a frog has just ceased contracting, a stimulus is applied, it replies at once by a second contraction. During contraction, heart muscle is refractory, i.e. it will not respond to a stimulus, and when the normal stimulus arrives from the sinus, the heart is refractory as the effect of the artificial stimulus. Hence the next normal stimulus is ineffective, and no contraction will occur until the next after that arrives. This unduly long interval gives the appearance of a missed beat of the heart or pulse. It may be appreciated by the patient as a cardiac pause, or since the heart becomes unduly filled and contracts more forcibly after the missed beat, the next contraction may be felt as a thud in the cardiac region. A large number of individuals have extra systole, and are unaware of it. Nor is there any evidence

that the condition is of serious import, though a search should be made for a cause amongst those conditions well known to affect the heart. The condition must be differentiated from the dropped beat of partial heart-block, in which latter no ventricular contraction can be determined, whether by auscultation, by palpation in the region of the apex beat, or by instrumental means, whereas in extra systole these are present. By far the most serious state in which the pulse is irregular is that of auricular fibrillation.

Auricular Fibrillation.—In this condition the auricle contracts in an irregular and disorderly fashion, and for practical purposes ceases to act. Here we see quite clearly that the proper function of the auricle is not one necessary to life. The ventricle fills in virtue of its diastole and the slight pressure in the veins. There is no actual suction, for the veins would readily be sucked flat, since they have such thin walls. The function of the auricle is subsidiary to a system for the collection of blood. By adding a small quantity to the already filled ventricle, the tension within the latter is increased, a procedure which makes it contract more forcibly. In this condition it would appear to be an irregular destruction of some of the auricular fibres, as a result of disease, drugs, or overstretching, from too high an internal pressure, as in valvular disease. It is well known that the condition is specially liable to supervene in certain types of valvular disease, e.g. that of the mitral valve, especially mitral stenosis, in which most strain is thrown on the right side of the heart. In such a condition, the auricle may readily find itself attempting to add to the contents of an already filled or overfilled right ventricle.

For our present purpose, however, it is evident that such irregularity of auricular contraction must lead to irregularity of conduction. The impulses sent out from the pace-maker reach the auriculo-ventricular node irregularly, and the ventricles as a result contract irregularly. The pulse is then characterized by an irregular irregularity, which distinguishes it from other forms of cardiac irregularity. The degree to which the condition influences the heart depends on the general state of the cardiac musculature, which is more fully dealt with in Chapter XVII. Once established, auricular fibrillation seldom disappears, although the patient may live a moderate life for a long period subsequently. More often, cardiac failure is not far distant, and existence, if it continues, becomes very limited.

Auricular Flutter.—Another condition of interest in relation to the auricle and pulse, is auricular flutter, first described clinically by Jolly and Ritchie, although it had been previously demonstrated by MacWilliam. Here we have a condition which may be looked upon as somewhat similar in nature to auric-

ular fibrillation, but much less severe. As a result of possible local injury, there is a delay when the stimulus reaches certain areas of the auricle, which therefore contract later than the rest of the organ. The late contraction of the localized areas may cause the whole auricle to contract once or twice or even three times between the normal stimuli sent out by the pace-maker. Lewis has described the condition as a "circus" movement. The auricle then goes on at a greatly increased rate, perhaps three to four hundred per minute. All these impulses, however, cannot pass down the auriculo-ventricular bundle, and stimulate the ventricle. There is, then, some degree of heart-block, for only a proportion of the impulses is affected. This yields a three to one, or more usually a two to one rhythm between the auricle and ventricle.

The pulse is commonly over 150 per minute in such cases, and may be irregular. A simple instrumental examination with the sphygmograph will make it evident that there is a regular irregularity as in sinus arrhythmia, except that the grouping does not correspond to the respiration. Obviously this is due to the fact that the abnormal stimuli which bring about the abnormal rhythmic contractions take a constant time to travel thither, and differ from the normal pace. They may, however, coincide occasionally, just as two tuning-forks produce beats, when of slightly different pitch. This occasional coincidence occurs at regular intervals, and so produces a grouping. It must, however, be admitted that it is difficult to make out this rhythm, and often the polygraph or electrocardiograph is necessary.

THE CHARACTER OF THE PULSE

The general character of the pulse is one which can only be appreciated by practice, and even then it must be clearly recognized that such clinical observation is very liable to fallacy. The normal pulse should rise and fall gradually, and should be fairly well sustained, while there should be no waves appreciable in the falling away. This is to be expected from the driving of a wave of the nature of that produced by the muscular contraction of the heart through an elastic system. Several conditions, however, lend a special character to the pulse wave. If the aortic valve is incompetent (and associated with this condition is arterio-sclerosis, and increased peripheral resistance), the pulse wave may be expected to have certain definite characters. The wave is a large one, for not only does the heart put out the normal amount of blood, but also that which has regurgitated into the ventricle. It is forceful, in virtue of the fact that the ventricle has hypertrophied. Also the arterial system is more rigid than normal, and this further accentuates the wave. On instrumental exam-

ination with the sphygmograph, the up-stroke is seen to be abrupt. In view of the incompetence, the wave falls away extremely rapidly, especially if the arm is held up vertically. A sudden and forceful pulse is produced, and may even be evident in the visible arteries, such as the temporals or carotids. This has been called the Corrigan pulse, from the physician who first described it, or a water-hammer pulse, from its resemblance to the sensation produced by the well-known scientific toy of that name. In aortic stenosis, on the other hand, in which there is resistance to the outflow of blood from the left ventricle, the pulse has a small amplitude, and is slow in its rise and fall.

When the blood pressure is low, there is a rapid rise and fall of the pulse wave, but the amplitude is smaller. A well-marked dicrotic notch on the downward stroke may be seen or appreciated with the fingers. This is due to the fling-back of the aortic valves, and the subsequent wave which is produced, as a result of the closure. The old physicians used to consider that the pulse gave an indication of the cardiac output, but from what we now know of the physiology of the heart, this can no longer be considered to be so. The character of the pulse depends entirely on the nature of the wave produced, and the state of the system into which it is sent. Thus, in a high blood pressure with rigid arteries, there is an abrupt rise but a comparatively small one, and as the blood does not escape readily from the large arteries there is a very slow falling away. Such a pulse is described as a "wiry" one. On the other hand, relaxed arteries (with a low blood pressure) and a weak heart, yield a very small pulse which may scarcely be appreciated, and which is described as "thready" and "running."

It must be clearly understood that the character of the pulse in no way depends on the rate of the pulse wave. This latter is dependent on the elasticity of the arterial walls.

THE HEART SOUNDS

The character of the heart sounds has long been recognized as an observation of considerable clinical importance. There are two sounds, which have been aptly compared with that represented by "lubb-dup," the first being long and of low pitch, while the second is lower and sharper. A third sound occasionally occurs, but is of little practical importance (see page 109).

The first sound is caused by the closure of the auriculo-ventricular valves, and the contraction of the ventricular muscle. The latter fact is obvious, since the sound may still be heard on listening to the empty excised heart (or even a voluntary muscle), when it contracts. The sound which marks the begin-

ning of ventricular systole is then essentially muscular in nature, for the force of the closure of the auriculo-ventricular valves depends on the ventricular contraction. These valves have already been floated into the position of closure by the accumulation of blood in the ventricle. The manner of its production is of first importance, as it gives a valuable indication, even if the sound is impure, of the state of the musculature of the main chambers of the heart. In fevers, for example, or in myocarditis, faintness of the first sound, if of recent onset, is evidence of cardiac impairment, and demands rest in a recumbent position. When, however, the chest is fat or the lungs are voluminous, it may be difficult to hear even normal breath sounds; indeed it may only be possible by asking the patient to hold his breath in expiration. In such circumstances the relative intensities of the first and second sound at the cardiac apex are of value. The first sound is best heard in this region where the ventricle abuts against the chest wall, and it may still further be increased by getting the patient to lie over on his left side. Should there be any difficulty in differentiating it from the second sound, this may be done by palpating the arterial pulse in the neck, with which it is practically synchronous. In the region of the apex, usually in the 5th intercostal space, 3½ inches from the middle line, the first sound should be louder than the second, and if this is not so, the first sound is weakened or the second exaggerated. Between these two the blood pressure will differentiate as described below.

Similarly, if the heart muscle is hypertrophied, the sound is accentuated and assumes the character of a sustained muffled thud, as would be expected, since the valves are closed more forcibly, there is increased muscle, producing a sound, and from the fact that the sound has to pass through thickened musculature. When the heart has been dilated the walls are thinner, and the sound, though exaggerated, is clear, sharp, and of higher pitch.

The clearness of the first sound is masked when the auriculo-ventricular valves are at fault. This commonly occurs at the mitral valve. The character of the sound then becomes blowing, and more closely resembles the sound of the word "luff." This alteration constitutes a cardiac murmur or bruit. The commonest auriculo-ventricular murmur is the mitral systolic, which occurs in cardiac systole and is the result of impairment of the mitral valve. It is best heard in the region of the apex beat. Hence this apical area is often known as the mitral area, though it is to be noted it does not cover the area of that indicating the surface marking of the valve. It is merely the point at which the ventricle comes nearest to the surface. Such an impairment may result from actual valvular disease, or from stretching of the valve which permits

regurgitation of the blood, although in the latter instance there will always be evidence of disease of the aortic valve. In the case of the impairment being due to conditions in the tricuspid valve, the murmur is heard best in the tricuspid area, which is over the lower part of the sternum. Here the regurgitation is almost invariably the result of cardiac dilation and the result of earlier disease elsewhere.

The first sound may also be masked by any condition which obstructs the exit of the blood from the aortic valve, or, more commonly, which brings about dilatation of the aorta beyond the valve. This murmur, in virtue of the nature of its production, is much rougher than that due to mitral regurgitation and has its point of maximum intensity over the aortic area. Further, it is conducted in the direction of the blood flow and may be heard in the arteries of the neck.

In the consideration of cardiac murmurs it must not be forgotten that even in anæmia, debility, or in conditions of excessive heart action, as in exophthalmic goitre, a systolic murmur may accompany the first sound. Apparently these murmurs are due to the decreased viscosity of the blood setting the valves in motion, and possibly to dilation with subsequent regurgitation, but admittedly the nature of their production is not quite certain. Such murmurs are always systolic in time and of a soft blowing character. They may be produced in any valve, but are more commonly found in the pulmonary area in the second left intercostal space, where murmurs produced at the pulmonary valve are best heard. They tend to be inconstant, but can be elicited by exercise. It may here be noted that systolic murmurs in the pulmonary region due to actual changes in the valve are seldom found except in congenital stenosis of the valve in which they are associated with patency of the foramen ovale or dilatation of the pulmonary artery.

The loudness of systolic murmurs, like that of the first sound, depends on the state of the cardiac muscle. Hence a faint murmur does not necessarily indicate the small amount of regurgitation, but rather a weak muscle. Confirmation of the diagnosis will depend on evidence of distress produced by exercise.

The second cardiac sound occurs at the beginning of diastole and is due to the closing of the pulmonary and aortic valves. These valves are already in a position of closure as soon as the expulsion of blood from the ventricles ceases and are firmly closed as the result of the elastic recoil of the arteries. It is best heard in the aortic area or the second right costal cartilage where the aorta is nearest the surface and, as in the case of systolic murmurs, produced

at the aortic valve, can be heard especially if accentuated in the large arteries of the neck. The intensity of the second sound, just as we have seen in relation to the first sound, depends on the force with which the valves are closed. An accentuated second sound is to be expected in conditions where the arterial pressure is high and indeed is a useful adjunct in the diagnosis of such conditions. Normally, in the aortic area, the two sounds have almost equal intensity and have rather a "tic-tac" or "lubb-dub" rhythm.

Should, however, the aortic valve be diseased, the character of the second sound is quite changed, and instead of being like the syllable "dup," is better imitated by "duff." For practical purposes only, the aortic valve need be considered in this respect, as a pulmonary diastolic murmur is of extremely rare occurrence. It has been described as a result of excessive pressure in the pulmonary artery as in mitral stenoses. Such an aortic murmur is produced by regurgitation of blood into the left ventricle during diastole. It is then propagated in the direction of the flow of regurgitating blood and may be heard all over the præcordia. The heart itself and the sternum may also play a part in its conduction; indeed, the point of maximum intensity of a murmur is often on the left side of the sternum. Like all sounds produced at the aortic valve, it is well heard in the aortic area. Commonly, however, when there is aortic obstruction, there is also some regurgitation of the valve itself, and a double see-saw-like murmur with the characteristics of each is heard. Such a condition obviously throws great strain on the left ventricle, which has not only to expel more blood, but has to do so against an increased resistance. If the left ventricle dilates and the mitral valve becomes incompetent, additional work is then thrown upon the right side of the heart, and a hypertrophy of all the chambers of the organ then takes place. It may, indeed, become so large that the term *cor bovinum* has been applied. From the point of view of prognosis, aortic disease, especially aortic regurgitation, is by far the worst form of valvular impairment.

Another murmur heard in late diastole, occurs in mitral stenosis. The auricle, it will be remembered, simply drives home the charge as it were into an already filled left ventricle and this occurs just before the ventricle itself contracts. We may consider that in the filling of the ventricle the blood does not flow through the valves sufficiently fast to produce a sound which is only made when the speed is increased as the result of auricular contraction. The sound produced by the blood passing through the stenosed valve is like other obstructive murmurs, extremely rough and purring in character and is almost fused with the first sound which becomes exaggerated. An imitation of the

sound is produced in the syllable "rupp," or, as is more common, if there is also regurgitation through the impaired valve, by the word "ruff." For this reason the late diastolic murmur is commonly referred to as being presystolic to distinguish it from true diastolic murmurs produced at the base of the heart, although less commonly, when the auricle is weak, the murmur is only heard at the time of maximum ventricular dilation, when it is really diastolic in time.

Very often one or more valves are impaired, and it is only by clinical experience and detailed study of the points of maximal intensity, the direction of the propagation of the murmur, the size of the cardiac chambers as elicited by percussion, and the patient's symptoms, that it is possible to decide the exact nature of the lesion present. In obtaining accurate diagnosis of the impairment of individual valves clinical observation has proved itself to be of the greatest possible value and is not surpassed by any other means. The character of the heart sounds only gives, however, a very limited amount of information regarding the cardiac musculature, and it is now realized that although such accurate diagnosis may be a guide in treatment and in the making of a good prognosis, yet a study of cardiac sounds is of little value in estimating the efficiency, with any degree of accuracy. It may, however, be useful in following the progress of an individual case.

Precardial sounds are not necessarily endocardial. In pericarditis, there is a rough see-saw sound produced by the rubbing of the pericardium upon the epicardium, but the rhythm and roughness taken together with the symptoms are usually sufficient for diagnosis. Similarly, a pleurisy in the region of the heart may be confused with a cardiac murmur, but in this instance the sound is related to respiration and not to the beat of the heart.

CHAPTER XIII

THE VENOUS PULSE. THE ELECTROCARDIOGRAPH

THE VENOUS PULSE

This refers to the pulse found in the great veins of the neck just above the clavicle. A variety of factors affect the detailed character of the pulse wave. The chief one is produced by the contraction of the right auricle, and hence the reason for taking records of the venous pulse as a help in clinical diagnosis. It gives the rate of the right auricle, and some indication of its force and rhythm, just as the arterial pulse gives information regarding the left ventricle.

Venous pressure is so low that it cannot be palpated, and instrumental methods of recording have to be used, the most practical being the polygraph, first introduced by Mackenzie. By its means the venous and arterial pulse may be simultaneously recorded. The writing system consists of two tambours activating two ink-writing levers, working at different levels. One tambour is connected by rubber tubing with a lever applied to the wrist to record the radial pulse, and the other similarly to a cup which is applied over the internal jugular vein, just above the inner end of the clavicle, at which point in the veins the valves have not yet commenced. The placing of the patient in a recumbent position increases the pressure in the neck veins and makes the pulse more easy to record. This, however, may not be necessary where there are greatly distended veins and the venous pressure high. It is no doubt true that such a method of recording venous pulsations as compared with optical methods, is relatively crude. Although the records may not be sufficiently accurate for scientific investigation, there can be no doubt that the polygraph is sufficiently accurate for many clinical purposes for which it is required and which are mentioned above. Characteristic tracings taken by the polygraph are shown in Plate IV, but although it may be comparatively easy to differentiate the various waves of a jugular pulse in a normal individual, difficulty necessarily arises in the interpretation of less typical and abnormal pulses, in which there is doubt regarding the movements of the auricle. A short consideration of the cause of the waves is necessary before the principles of the interpretation of the polygraph records can be given. The usual nomenclature adopted by Mackenzie is adhered to.

The first wave, known as the *a* wave, is caused by the contraction of the auricle and the cessation of the venous flow into the heart from closure of the venous inlet which is surrounded by auricular fibres. There is some difference of opinion as to how the auricular contraction causes the wave, but the main fact that it does correspond to auricular systole is not disputed. The latter normally occupies about a tenth of a second, and if it is longer a complicating factor must be sought. The *a* wave is followed after a fifth of a second by the *c* wave.

This second or *c* wave has also been the cause of considerable controversy. Mackenzie held that it was due to transmission of the carotid pulse to the vein. Staub considers it to be due to systole of the right ventricle raising the auricular floor, for a rise in pressure synchronous with ventricular systole is found if the pressure is taken in the right auricle. Starling has found an apparently corresponding wave in the inferior vena cava. The work of Wiggers, who has used very sensitive recording apparatus, appears to show that although there is a rise in auricular pressure during ventricular systole, the wave produced is not necessarily communicated to the veins, even when it does precede the *c* wave. He concludes that the latter is produced by the pulsation of adjacent arteries, not only in the neck but also in the thorax. This latter accounts for the corresponding wave found by Starling. Whether the wave is transmitted by the vein or artery does not fortunately make any difference to the fact that the *c* wave is produced by ventricular systole. By being so fixed it is the point from which all interpretation of the venous tracing can be made.

The *v* wave is the result of blood collecting in the right auricle, while the tricuspid valve is still closed. The subsequent fall is due to the opening of the tricuspid valve and the free passage of blood into the right ventricle. Since the *c* and *v* waves approximately mark the beginning and end (really the beginning of diastole) of ventricular systole, the interval between the *c* and *v* waves must be of fixed duration.

The simplest conception of what is occurring in the right auricle is that of a rise and fall of pressure, or a simple wave, brought about by the filling, the contraction, and later the dilatation of the chamber. The latter is interrupted by the *c* wave which corresponds to ventricular systole. The up-stroke of the wave or the rise of pressure in the auricle is similarly interrupted by the opening of the tricuspid valve causing the notch *y* and the *v* wave preceding.

In such interpretation as mentioned above, the starting-point is the *c* wave, which occurs one-tenth of a second before the rise of the wave of the radial pulse. They are of common origin, both being produced by ventricular systole,

the difference in time being merely due to the fact that the radial pulse wave has further to travel. If, then, a point has been marked one-tenth of a second before the rise of the radial pulse, the corresponding point in the auricular tracing is the beginning of the *c* wave. Simultaneous points in each tracing may readily be denoted by stopping the movement of the paper for a moment.

Normally the wave in such an auricular tracing which begins a fifth of a second before the *c* wave is the *a* wave, and the space between is known as the *a–c* interval. If the wave begins before this point, then the *a–c* interval is considered to be lengthened. This is taken as an indication that the stimulus has taken longer than normal to pass from the auricle to the ventricle.

Similarly, if a point two-fifths of a second after the *c* wave be measured, the point is approximately the summit of the *v* wave and should fall almost at the bottom of the dicrotic notch in the radial tracing, as the closure of the aortic valve, to which the dicrotic notch is due, occurs approximately at the same time as the tricuspid valve opens, i.e. at the beginning of ventricular diastole. The *v* wave is usually well marked and may, indeed, be the most distinct wave in the auricular tracing. It will be noted, too, that the *a–c* interval is constant for any given heart, as it marks the beginning and end (really the beginning of diastole) of ventricular systole. This period does not vary appreciably whatever the rate of the heart, for any alteration in its rate is for the most part brought about by a difference in the duration of diastole.

Any other waves which occur in the auricular tracing are considered to be due to extra auricular or ventricular contraction. There is, however, one fallacy to be remembered, namely the *h* wave, so called as it was first described by Hirschfelder. Gibson attributed it to the temporary closure of the bicuspid valve by eddies caused in the filling of the right ventricle. To this closure, also, has been attributed the third heart sound, which is occasionally heard. An *h* wave may occur obviously between *a* and *c* during which time the ventricle is filling, but in a rapidly or slowly-beating heart may add confusion (being taken for an extra beat of the auricle). This may cause a diagnosis of heart-block to be made, while in a real heart-block the *h* wave, if it occurs after auricular contraction, may be taken for a normal *c* wave. More commonly, however, it occurs between *v* and *a*, and here it may obscure the *a* wave itself and cause the *a–c* interval to appear long, but it will be seen that in this case the duration of the auricular wave will be longer than the normal tenth of a second.

Normally, the number of *a* waves should correspond to the number of *c* waves, but in several conditions this is not so. These have already been dealt

with in relation to the pulse and need only be summarized. In heart-block the auricular rate is about normal, while the rate of the ventricle is slow, often half or a quarter of the rate, or at an early stage there may be merely an increase in the *a–c* interval beyond the normal fifth or, according to Lewis, third of a second, which indicates a delayed conducting mechanism from the auricles to the ventricles. In auricular flutter, on the other hand, there may be an enormous number of *a* waves, and only a proportion of these is followed by *c* waves, while in auricular fibrillation there is no regular *a* wave at all. In extrasystole it will be seen that an auricular contraction, followed by a ventricular contraction, takes place before the normal auricular contraction is due. The diagnosis of this latter condition, however, is, as indicated on page 99, sufficiently clear from the examination of the radial pulse, when the compensatory pause will especially be noted.

THE ELECTROCARDIOGRAPH

In the early days of electro-physiology, it was the custom in certain quarters, to criticize the teaching to medical students of what seemed at the time to be a useless physiological phenomenon, namely the current of action of a muscle. To-day the latter is the basis of electrocardiography.

If two electrodes connected with a galvanometer are placed on a muscle, then when it is made to contract, it will be found that a momentary current passes through the instrument from the normal to the contracting part of the muscle. This is known as the current of action. In electrocardiography we record the current of action of the heart, and from the records are able to obtain evidence of the contraction of its different parts. The speeds with which the different chambers of the heart contract make it at first very difficult to record the action current. Since the introduction of the string galvanometer by Einthoven in 1901, the matter has become comparatively easy. The galvanometer consists of a string of silvered quartz or in the more modern forms of a gold-splattered glass fibre suspended between the poles of an electro-magnet. A portion of the fibre is so illuminated that the shadow of its movements can be recorded on a moving photographic plate. A typical record is seen in Plate IV. In man the currents cannot be obtained directly, but may be obtained indirectly by attaching the leads from the galvanometer to the limbs by large non-polarizable electrodes. Three standard leads are commonly used. Lead 1 is from the two hands, lead 2 from the right hand and left leg, and lead 3 from the left hand and left leg. Commonly, the limbs are placed in a bath of saline solution into which dips a porous pot containing zinc sulphate and zinc electrodes which

PLATE IV. Combined Polygraphic and Electrocardiographic Records (Flint).

lead to the galvonometer. The accurate interpretation of such records we owe, to a very large extent, to Lewis and his co-workers.

The first wave P of the electrocardiogram is positive and is due to auricular contraction. Following the auricular wave is the ventricular complex of waves Q, R, S, T, and much discussion has taken place as to the cause of these. It is generally accepted that the Q wave is due to the contraction of the papillary muscles when this wave is seen, and it has already been noted that the Purkinje fibres in which the bundle of His terminates is specially applied to these muscles. As would be anticipated also, it is essential that these muscles should contract at the very commencement of ventricular contraction if they are to prevent the auricular-ventricular valves from being blown backwards into the auricles. The R wave is due to the contraction of the ventricle, but when the apex contracts, its stronger negativity opposes the current produced at the base and the S wave is produced. The contraction, however, passes off sooner at the apex than at the base, which again becomes negative to the apex and brings about the T wave. A still later deflexion V has been described and is related to diastole.

In the electrocardiograph, as in the polygraph, the main point is the recording of auricular contraction relative to that of the ventricle, and if P be substituted for *a*, and *c* for the R wave, what has already been said in relation to the polygraph applies to the electrocardiograph. It will be evident, then, that the P–R interval in the electrocardiograph corresponds to the *a–c* interval of the polygraph, and it is considered that this interval normally does not exceed a fifth to a third of a second.

Hypertrophy of the various chambers of the heart may be indicated from the size of the waves produced, as shown by Lewis, from a study of electrocardiograms taken in animals, in which the auriculo-ventricular bundle has been cut, thus altering the ventricular rates. It has thus been found that the left ventricle is chiefly responsible for the R wave in lead 1, and S in lead 2, while the right ventricle accounts for S in lead 1 and R in lead 3. As the production of current depends on the amount of muscle, the size of the waves in the various leads indicates the amounts of musculature at work. For comparative purposes the galvanometer is so standardized that the string moves one centimetre for each milli-volt potential difference.

All that has been written regarding the various conditions which affect the pulse should be read in relation to the electrocardiograph and polygraph. The former instrument has the great advantage over the latter in that so far as the *a* wave especially is concerned, it is affected by fewer factors than the *a* wave of the polygraph. It records only the results of muscular contraction, while

the polygraph records are influenced appreciably by the cardiac valves. Since the use of the electrocardiograph is so specialized in its practical aspects, only the broadest outlines of the subject are given here. Those who wish for more information are referred to special treatises on the subject, such as that of Lewis. Although the apparatus is costly, there is nothing excessively difficult in its manipulation.

CHAPTER XIV

BLOOD PRESSURE

The clinical term pressure is usually reserved for that in the brachial artery. It is indicative of that in the arteries generally, although it varies from artery to artery. This, however, gives no information as to the pressure in the capillaries and veins. Blood pressure as measured clinically bears an approximation to that determined experimentally. The latter is found quite accurately by putting a cannula into an artery and connecting it to a manometer by a tube containing some anti-coagulant fluid. In clinical practice we have to be content with finding that pressure, which applied to a limb (usually the arm) by an inflatable rubber armlet will just obliterate the pulse. Such a method can only be approximate, for we have to neglect variations in the nature of the tissues of the arm compressed, and in the wall of the artery. We can readily appreciate the former fact by finding the difference in the readings shown by applying the armlet to the upper arm and the forearm. Every attempt must then be made to insure flaccidity of the muscle in making the estimation. It is also necessary to have not only the body but also the mind at rest. The rate of the heart is an important and convenient guide in regard to the latter.

Clinical observation of a large number of persons shows that on an average, in the young adult, there is required an armlet pressure of 110 to 120 mm. of mercury to obliterate the radial pulse. This is the systolic pressure, or the pressure in the brachial artery at the end of cardiac systole. The pressure in the artery during cardiac diastole, known as diastolic pressure, is still more difficult to estimate, as the variety of methods used indicates.

The function of the blood pressure, like that in water or gas pipes, is to maintain a proper distribution throughout the area to be supplied (in the case of the body, to every tissue), under very varying circumstances.

The factors upon which blood pressure depends are: the pumping action of the heart; the peripheral resistance offered to the outflow of blood from the arteries together with the elasticity of the arterial walls; and the volume of the circulating blood.

The Heart.—Experimentally, it is an easy matter to show that the heart plays a part in the maintenance of blood pressure. Stimulation of the vagus,

applications of cold or heat to the pace-maker, or the injection of any cardiac poison, causes the blood pressure to fall at once. Clinically we obtain a low blood pressure from similar reasons when the cardiac musculature is poisoned by the toxins of disease, depressed by cold, or impaired by deficient action of the valves, or fatty degeneration. In these conditions the drugs known as cardiac tonics are especially valuable.

The Volume of the Blood.—The effect of variations in the volume of the circulating blood is not at first sight apparent, as the addition to or removal of small quantities from the blood-stream makes no appreciable difference to blood pressure, even experimentally. In man, fluid is normally added to the blood from the alimentary canal, and is removed by the kidneys, lungs and skin (Chapter XXXIII). The provision of a means of maintaining blood pressure in spite of a moderate degree of hæmorrhage forms one of the primitive protective mechanisms of the animal body. When the blood loss is sufficient to lower blood pressure, it is sufficiently obvious to make the actual taking of the blood pressure unnecessary. The blood volume may, however, be reduced relatively although not actually, as when there is a marked increase in the capacity of the vascular system. This is seen in the condition of histamine or in secondary wound shock. The condition of shock is of such great interest and is such a distinct symptom complex that it is dealt with in a special chapter (page 123).

The Peripheral Resistance and the Elasticity of the Blood-Vessels.—At each beat of the heart there is expelled into the arterial system a quantity of blood, but if this system were rigid not only would the pressure in the arteries fall to zero between the beats, but the flow from the system would be intermittent. In order to provide a steady outflow from the arteries at a high pressure, advantage is taken of a mechanism seen commonly in use for the same purpose as in scent sprays, bagpipes, and fire engines. A resistance is offered to the outflow of blood, so that more is pumped into the system during each beat of the heart than can escape from it in the same time. The extra blood is accommodated by having the system elastic and the recoil of the walls, which are stretched at each systole, maintains the pressure during diastole. The second bulb of the scent spray, the bag of the bagpipe, the compression chamber of the fire engine, together with a nozzle in each instance, provide a similar arrangement for maintaining a constant flow at a high pressure. In the body, but for the constant flow, we should be conscious of the pulse at our various nerve endings, a fact which we can readily appreciate on inhaling amyl nitrite, when a throbbing in the head may be felt. Patients with arterio-sclerosis,

whose arteries are more rigid than normal, frequently have throbbing sensations which often interfere with sleep. The throbbing of an inflamed part of the body is also partly due to local dilation of the peripheral resistance and the permitting of the pulse to be continued through into the capillaries in the vicinity of the nerve endings. In this instance, the swelling of the tissue may play a part in making the pulse directly transmissible from the artery to the nerve ending. The peripheral resistance is situated for the most part in the small arteries and arterioles, in which the cross-section of the vascular system is noticeably reduced. That there is a small amount of resistance in the capillaries seems likely, but there are indications that this is only appreciable when the arteries are dilated.

Any constriction of the arterioles will then, by increasing the peripheral resistance, raise the arterial pressure, both systolic and diastolic. This is seen in various pathological states such as nephritis and arterio-sclerosis. In the latter condition, the lumen of the small arteries may become so reduced that little or no blood can pass through, with the result that in extreme cases gangrene or death of the part supplied may set in. In conditions of arterial disease in which the diastolic pressure is high, the heart has to do appreciably more work in evacuating its contents, and hence we commonly find in these conditions hypertrophy of the left ventricle, the finding of which may be a useful diagnostic aid in differentiating between a temporary or more permanent increased blood pressure. The multiple factors in the maintenance of blood pressure are often overlooked in this respect, for should the left ventricle not be equal to the task, there may be a normal or even a low blood pressure in spite of the greatly increased peripheral resistance which, as a result, may be overlooked.

In arterial disease too, there is a reduction of the arterial elasticity, and less blood can be accommodated in the arterial system than normal. There is, as a result, a noticeably greater thrust forward of the blood and greater tendency to an intermittent flow in the capillaries. We are also able to appreciate the characteristics of a high tension pulse. This is a combination in which the increased peripheral resistance and diminished elasticity play a main part, and in which the rise in the up-stroke as shown by the sphygmograph or felt on careful palpation, is abrupt but small. As the outflow from the arteries is slow, there is a slow down-stroke.

If there is diminished elasticity of the vessels, there is also a marked increase in the velocity of the pulse wave, as shown by Freiberger and by Munzer in 1912, since the velocity of the pulse wave depends on the elasticity of the arteries and the internal pressure. The velocity can easily be calculated from

the time of arrival of the pulse wave in the radial and carotid arteries, which is most accurately recorded by the hot wire sphygmograph of A. V. Hill.

The peripheral resistance may also be varied in different parts of the body according to its needs, to allow the part being utilized to receive a large supply of blood. Further, in conditions of blood loss, whether actual or relative, the peripheral resistance is increased in an attempt to maintain the circulation, especially in the coronary arteries and brain (see Chapter XV).

This indicates that the peripheral resistance is under a certain amount of control, and it is found to be from the vaso-motor centre in the medulla and subsidiary centres in the spinal cord. The mechanisms by which the peripheral resistance is varied, according to requirements, for the maintenance of blood pressure are now fairly clear and form an important means by which animals can adapt themselves to varying conditions of life, which demand exercise, changes of posture and the like. These are dealt with in relation to the Integration of the Circulation (Chapter XV).

In anticipation of exercise, however, the body prepares in advance, and increases the blood pressure, causing the distribution of blood to become more efficient. This increase of blood pressure is brought about by an increased cardiac output, indicated by the increased heart rate, and increased peripheral resistance. In such circumstances the increased resistance occurs particularly in those areas less likely to be required, namely the alimentary canal, its associated glands, and the skin. The vaso-constriction in the skin is often evident by pallor, and we talk about an individual being "pale and determined," "pale with fright," "having the blood run cold," etc. The latter condition is undoubtedly of the same nature as the sensation of cold experienced at the onset of febrile conditions, and is due to less blood being circulated near the nerve endings of the skin. Accompanying any vaso-constriction in the skin, is a fall in its electrical resistance (Aveling and McDowall). This fact is apparently the physiological explanation of what has been termed by the psychologists the "psycho-galvanic reflex," the presence of which is an indication of the emotive response of the individual to the stimulus. Later in the exercise, however, when the sweat glands which are under the influence of the heat-regulating centre (see page 283) become active, the skin vessels dilate. A similar action may be seen experimentally if pilocarpine is injected into an animal when there is at first instance vaso-constriction, e.g. of the pad of the foot, from direct action of the drug, but later on, when sweating commences, there is dilation of vessels, no doubt from the effects of the metabolites. In general, once the exercise has

commenced, any vaso-constriction in unused parts is counterbalanced by the dilation in other parts.

This response to anticipation of exercise opens up many considerations in relation to the ætiology of high blood pressure as a result of intense mental activity, but as yet there is little certainty in the matter. Suffice it to say, that habitual over-action of the arterial wall would presumably lead to hypertrophy, and this, if excessive, would bring about increased peripheral resistance.

Pulse Pressure.—Various clinical observers have attempted to draw definite conclusions regarding the exact significance of pulse pressure, or difference between the systolic and diastolic pressures, especially in relation to the output of the heart. Various formulæ have been devised by which the output of the heart has been said to be estimated by observations made on the pulse pressure together with the heart rate. No consensus of opinion has been reached, nor indeed does it seem possible so long as the filling of the heart as indicated by the venous pressure is neglected. If the venous pressure is low, large variations in the rate of the heart may occur and the output remain the same, but, since normally, the venous pressure is such that the heart is fully filled in a shortened diastole, an increase in the rate of the heart itself affects the output. For example, the increased heart rate which occurs in anticipation of exercise, or in emotion, is associated with an increased cardiac output per minute, and is to a considerable extent responsible for the raised blood pressure which occurs in such circumstances. Pulse pressure is undoubtedly to a very large extent directly dependent on heart rate. The faster the heart, the less time the systolic pressure has to fall before the next systole.

Of special importance is the significance of the pulse pressure in relation to blood pressure, and several definite facts are brought out experimentally. Thus a high blood pressure associated with a low pulse pressure is probably due to the cardiac acceleration found in the conditions just mentioned.

Difficulty arises, however, in the very cases where information is desired, namely, in those of high blood pressure. A simple increased peripheral resistance, as may readily be shown by mechanical circulation, results in a high blood pressure together with a small pulse pressure. This, however, is complicated clinically by the fact that, as a rule, in cases of high blood pressure the pulse is slow, since, as we know, such a pressure in the aorta and right side of the heart stimulates the endings of the depressor nerve and thereby the vagus centre to bring about slowing. This slow heart causes the pulse pressure to be increased and is commonly seen clinically in cases of high blood pressure. It is probably a good sign in regard to the efficiency of the heart. Later, however, where the

heart begins to fail, e.g. from fatty degeneration, the effect of the increased venous pressure resulting from the weakened heart brings about an increased heart rate which, as we have seen, now reduces the pulse pressure.

In view of the fact, then, that not only are the heart rate and peripheral resistance variable and that the blood pressure may be affected by the varying of either, it is difficult to see how any accurate conclusion can be arrived at from a study of pulse pressure. The only significant observation in this direction appears to be that a rapid heart and low pulse pressure not due to any other obvious cause and accompanied by palpable thickening of arteries probably indicates an impaired heart.

Venous Pressure.—There can be little doubt that the value of venous pressure as an indication of the state of the circulation has by no means been adequately studied. Experimentally, it can readily be shown, that the venous pressure gives a very accurate idea regarding the state of the heart. Any failure of the heart shows itself by a rise in venous pressure long before there is any fall of arterial pressure, as the latter, when due to cardiac causes, is prevented to a large extent by increased peripheral resistance. Similarly, any dilation in vessels, such as by alcohol or histamine, is, apart from the transient effect of the latter, indicated by a prolonged fall of venous pressure, although that of the arteries may remain unchanged. Clinically, the means used for its measurement are the amount of pressure necessary to compress a vein over which is sealed a glass capsule in which the pressure may be raised (von Recklinghausen) or by the actual putting of a cannula into the vein and attached by means of a sterilized non-coagulant fluid to a manometer, preferably aneroid (Bedford and Wright). The second method, no doubt, gives the most accurate value, but is a little inconvenient, and the first, although perhaps less accurate in this respect, gives relative values, especially in a given case. It will be obvious that it is essential when taking such pressure to have the patient always in the same position. There is, as shown by Hooker, some small diurnal variation and an increase with old age, as in the case of arterial pressure, but more recently Eyster and Meek have emphasized its value as a source of useful information regarding the heart. The writer can certainly support this from an experimental standpoint.

CHAPTER XV

THE INTEGRATION OF THE CIRCULATION. THE EFFECT OF HÆMORRHAGE AND ALLIED CONDITIONS. THE NATURAL ARREST OF HÆMORRHAGE

THE INTEGRATION OF THE CIRCULATION

The integration of the circulation is brought about by a large variety of mechanisms, the elucidation of which we owe largely to Bayliss, Dale, Langley, Starling and their co-workers.

In the chapter on "Blood Pressure," some of the mechanisms concerned in its maintenance have been pointed out, and it has been noted that each of the factors on which it depends is variable. Unfortunately, it has become the custom to consider various parts of the circulation separately, and to study the control of the heart, of the blood-vessels, and of the capillaries somewhat apart. This is but the natural result of methods by which the various facts have been isolated. It must, however, be realized that they are but part of one mechanism for the blood supply of the body and especially the muscles, and it will be seen that the circulation and respiration (although the central processes of life as a clinical entity) are, in reality, the servants of the rest of the body.

When a muscle becomes active, lactic acid and carbon dioxide are produced together with substances which cause a dilation of capillaries locally. It has been clearly shown by Krogh, that in an active muscle very many times the number of capillaries in use during rest are opened up. Individual tissues vary appreciably in this respect. In addition to the substances just mentioned it seems probable that other metabolites of protein akin to histamine (which has been shown by Dale and Richards to dilate such vessels) may also have a vasodilator action.

In addition, there are quite definitely reflex mechanisms capable of dilating the vessels in active tissues, and it is probable that the importance of the Lovén reflexes have been overlooked. The stimuli apparently arise within the active organ itself, and bring about reflexly a diminution of the normal arterial tone.

It will be evident that in the event of certain tissues taking more blood in this way, and since the amount of blood in the body is limited, it will become necessary for those organs which are not required to close down. There seems

to be little doubt from the well-known effect of asphyxia, and from the relationship of carbon dioxide to the vaso-motor centre, that this reduction of the blood supply to inactive tissues is brought about by the carbon dioxide produced by the active tissue. This carbon dioxide not only acts directly on the veins (and the veins of the abdomen can contain about a third of the blood in the body), but also indirectly upon both arteries and veins, in virtue of its action upon the vaso-motor centre in the medulla. The action of this centre is still further enhanced by sensory stimulation, should any occur, and as we have seen in relation to "Blood Pressure," even by anticipation of exercise. The lack of carbon dioxide will have the opposite effect, as we may readily experience if we forcibly overbreathe when the blood pressure falls,—the skin becomes pale, and we experience a sensation of giddiness. It also accounts for the extreme sense of weakness which may be experienced at high altitudes, as a result of the washing-out of carbon dioxide through the excessive action of a respiratory centre rendered hypersensitive by oxygen want, and may be concerned in "Surgical Shock" (*q.v.*).

The impulses from the vaso-motor centre pass down the spinal cord and pass out in the sympathetic outflow from the 2nd, thoracic, and 3rd, lumbar roots. In raising blood pressure experimentally by electrical stimulation of the splanchnic nerves, or injecting adrenaline, we are then but activating some peripheral parts of the mechanism.

We must associate such shutting down of inactive tissue with the action of the sympathetic nervous system. As was shown in relation to the "Rate of the Heart," muscular activity accelerates this organ by raising the venous pressure in the region of the pace-maker, thus diminishing vagus restraint and increasing sympathetic action (see page 91).

Thus we see that the carbon dioxide produced by the muscle during contraction, not only dilates its own blood-vessels, but closes down those of other tissues not in use and at the same time hastens the circulation and raises the blood pressure, which still further causes the active tissues to receive more blood. In severe exercise we believe the action of the whole mechanism to be still further enhanced by the action of adrenaline secreted as a result of the stimulation of the splanchnic nerves from the vaso-motor centre.

Another mechanism of importance in relation to the integration of circulation is the depressor reflex with which is closely associated the action of the vagus. At each beat of the heart impulses apparently pass up the depressor fibres of the vagus to its centre, which is stimulated, and to the vaso-motor centre, which is inhibited. Thus the heart is kept under restraint by the vagus,

while the action of the vaso-motor centre upon the blood-vessels is reduced. Experimentally, stimulation of the central end of the depressor may be shown to slow the heart by way of the opposite uncut vagus and to cause dilatation of blood-vessels. Conversely, section of the vagus brings about acceleration of the heart and general vaso-constriction.

The depressor mechanism may be looked upon as a means of safety whereby the heart is relieved should the pressure against which the left ventricle has to pump become suddenly excessive, as in strain or arterio-sclerosis.

Just as important, however, is the converse of the depressor reflex, namely a reduction in the depressor impulses as a result of reduced stimulation in the aorta and left ventricle. Such a condition will occur normally in the assumption of the erect from the lying position, and as such may be considered a vasculo-postural reflex, by which vaso-constriction and cardiac acceleration are brought about.

The Adaptation of Blood Pressure to Posture.—It is important also that blood pressure should be maintained reasonably constant in whatever position the body may chance to be. It is common experience that the sudden resumption of the erect posture from the recumbent is associated with dizziness, and a similar slightly more prolonged state of affairs is experienced after any illness which has confined one to bed. In such circumstances, the vaso-motor centre does not constrict the vessels, particularly those of the abdomen, sufficiently rapidly to maintain the pressure in the arteries, and the blood tends to remain in the dependent parts, causing a certain amount of cerebral anæmia. Yandell Henderson has shown that in man the output of the heart per beat is much reduced in the change from the recumbent to the erect posture. A caged rabbit or a snake may actually die if held in the vertical position for a time, as the blood fails to return to the heart. It is evident, then, that to be efficient the mechanism must be used. If the blood-vessels are diseased, as in arterial sclerosis, the response may be still less adequate and the individual suffers from giddiness.

In the beginning of a descent in a lift the sensations may be considered to be due to a temporary lack of adaptation on the part of the circulation, although here, no doubt, sensations are likewise experienced from the semi-circular canals. There is, however, rapid compensation. It is suggested, too, that sea-sickness is essentially of a similar nature, and that this is certainly true in some cases is strongly supported by the fact that an individual, although quite a bad sailor, may be quite normal in the recumbent position. The administration of cardiac tonics is a recognized form of treatment, while the well-

known fact that one becomes accustomed to the motion of a ship further suggests the formation of the reflexes. Why vomiting should result is difficult to explain except that it may be evidence of cerebral anæmia and akin to the vomiting seen in cerebral compression.

The pallor of cardiac cases is also vaso-motor in origin. It may be quite distinct, as in aortic regurgitation. In cardiac failure there is often a curious mixture of cyanosis and pallor, the congested veins being rendered more distinct by the pallor. This pallor is the result of vaso-constriction, again the result of a diminished cardiac output per beat, presumably by a lessening of the impulses which pass up the depressor to the vaso-motor centre.

THE EFFECT OF HÆMORRHAGE AND ALLIED CONDITIONS

When blood is lost from the body, provided the loss is not excessive, the blood pressure does not fall except during the actual time of the loss. Further fall is prevented by an increase of the peripheral resistance, and the general reduction of the capacity of the vascular system, together with an increased cardiac action. These are brought about reflexly. The actual fall of pressure, while it lasts, reduces the depressor impulses which at each heart-beat normally pass up the depressor fibres of the vagus to the cardiac centre. This brings about the increased rate of the heart and increased peripheral resistance. These two processes supplement each other and thus it is not necessary for the peripheral resistance to be increased to the extent which would otherwise be necessary. A certain amount of alteration in the peripheral resistance is thereby possible (should it be necessary) for the distribution of blood. There is also, no doubt, a direct stimulation of the vaso-motor centre as a result of the temporary fall of pressure in the cerebral arteries. The increased action of the heart and the arterial constriction reduces the amount of blood passing from the arteries to the veins, and causes a reduction of venous pressure. This has been shown by the author to cause impulses to pass up the vagus to the vasomotor centre and thus reflexly maintain the increased peripheral resistance. It seems most likely that the pressor influence of the vaso-motor centre extends not only to the arteries, but to the veins and capillaries whose capacity is reduced thereby, while Krogh considers that the liver may also become contracted.

At the same time there is a passage into the blood-vessels of fluid from the tissues which become dehydrated from reabsorption of lymph (Milroy), giving the face of the patient a shrunken appearance. The speed with which blood volume may be made up in this way is remarkable, and it is this which caused the old-fashioned treatment of bleeding to be given up.

If, however, the patient is bled sufficiently to reduce the arterial blood pressure 30 mm., it may be taken from experimental findings, that the lowering of the venous pressure is relatively three or four times as much. Further, so long as the arterial pressure is below its level, it may be rightly assumed that the venous pressure has by no means recovered. The relief which such a procedure will give to an impaired heart is obvious, especially when the cardiac embarrassment is enhanced by an abnormally high venous pressure, as is common in cardiac conditions. In such circumstances some clinicians still recommend bleeding to relieve the right side of the heart. The tissue fluids contain a greater number of immune bodies than normal blood, so that there may be more justification in bleeding than was thought.

In cholera, when the loss of body fluid is excessive, the blood volume may be reduced and the blood may become tarry in appearance. The symptoms are like those of hæmorrhagic shock.

Increased Capacity of the Circulation. Surgical Shock

There are few subjects on the borderline between physiology and surgery about which there has been so much controversy as surgical shock. Such discussion has been the result largely of attempts to attribute all forms of shock to the same cause, but gradually the position, with a fuller knowledge of the circulation, has become cleared.

The condition of shock is characterized by a marked fall of blood pressure, with all the signs and symptoms of blood loss without there having been an actual hæmorrhage. By practically all those who have investigated the subject, it is agreed that there is an increased capacity of the vascular system in some instances associated with increased arterial constriction, although how these may be brought about is not so evident. It is also agreed that the heart is not primarily concerned in the circulatory failure.

From what has been said in relation to the integration of the circulation, it will be clear that such a failure must be brought about in two possible ways: (1) by failure of the *vessels* peripherally to maintain their tone and normal permeability, or (2) by failure of the vaso-motor *centre* to maintain tone generally. It is practically certain that both possibilities may occur.

Peripheral Failure.—Evidence that wound shock, especially when delayed, may be due to substances produced by damaged tissues and capable of dilating the *capillaries* and increasing their permeability, we owe to the work of Bayliss, Cannon, Dale, Laidlaw, Richards and Wallace. Clinically it was observed that the amount of shock was closely related to the actual amount of tissue damage

brought about: further it was seen that patients suffering from injury to a limb to which a tourniquet had been applied were particularly liable to collapse when the tourniquet was removed, but the collapse did not occur if the limb was amputated before the removal. The fact that not infrequently the arteries were found to be markedly constricted indicated clearly that these vessels were not at fault. The final proof, however, that shock could be produced by a chemical substance was given by Dale and Laidlaw, who showed that such a condition could be produced by the injection of histamine. This substance, which is decarboxylated histidine, the latter being an amino-acid and a product of protein digestion, is found to occur in tissue extracts generally, is a normal constituent of the intestine, and is produced by B. coli even when grown in vitro. Histamine has been shown by Dale and Richards to bring about a profound dilatation of the capillaries, and later collaborators have demonstrated the increased permeability of these vessels.

It is not, however, claimed by these workers, as some writers appear to imagine, that all shock is due to the absorption of histamine-like substances, indeed there is ample evidence that shock may occur from other causes.

Central Failure.—As we have seen in previous chapters, the tone of the blood-vessels is kept up by the *vaso-motor centre,* the activity of which Dale and Evans have shown to be dependent on the carbon-dioxide content of the blood. It will be clear, then, that any condition which separates the centre from the vessels or which causes the carbon dioxide to be reduced must result in a fall in blood pressure from not only an increased capacity of the circulation, but also a loss of the peripheral resistance of the arteries.

Separation of the nervous connections of the vaso-motor centre may occur in spinal injury or disease in which shock is produced from interruption of the vaso-motor paths between the medulla and their points of exit from the spinal cord. Such an injury must, of course, obviously interfere also with impulses other than vaso-motor. The lower limbs may be affected while the upper part may be normal so far as voluntary movement is concerned (Sherrington). The effect on the blood pressure will depend on the extent to which the vaso-motor paths have been interfered with.

Porter has pointed out that fat embolism as a result of fracture of long bones may occur and there are many diverse ways by which the paths of the vaso-motor system may be interrupted. Rendle Short also has suggested that the primary condition in shock is loss of muscle tone resulting in lack of support of the blood-vessels. It is true that the rendering of the muscles flaccid by curare or by nerve section, if a sufficient amount of muscle is paralysed, does

cause a fall of blood pressure, for no doubt vaso-motor as well as motor fibres are affected. While it is agreed, then, that loss of muscle tone may exaggerate the condition and may be produced by spinal injury, it is clear that in other states loss of tone is secondary. This may indeed readily be shown experimentally by the injection of histamine or by the production of shock by acapnia (see below) in a decerebrate animal in which there is an excess of tone.

Of special importance in relation to central failure as a cause of surgical shock is undoubtedly sensory stimulation. This factor was first stressed by Crile and Mummery, who noted that shock was readily produced by excessive sensory stimulation, such as might occur after wounds or during operation under light ether anæsthesia. It was observed that often shock could be prevented by the block of the afferent nerves by local anæsthesia. Crile suggested that there was brought about by the excessive stimulation an exhaustion of the vaso-motor centre, but it can readily be shown that such exhaustion was not the primary cause, as the centre would still respond to sensory stimulation and particularly to the administration of carbon dioxide.

The real explanation has, however, been shown by Yandell Henderson to be due to the washing-out of carbon dioxide brought about by the hyperpnœa occasioned by the sensory stimulation. The *acapnia* or loss of carbon dioxide, as we have seen, brings about a reduction in the tone of the vaso-motor centre. It is extremely easy to produce such shock experimentally in an animal under light ether anæsthesia in which the stimulating effect of the ether upon the respiratory tract plays a part in addition to the effect of any operative procedure. In such anæsthesia, as pointed out by Henderson, it is important to remember that apart from the fall in blood pressure, there may be brought about death from failure of respiration as a result of the washing-out of the normal stimulus—carbon dioxide. The amount of this gas in the blood becomes insufficient to stimulate the partly anæsthetized centre and respiration becomes inadequate to supply the oxygen requirement of the body, especially of the heart and the medulla.

Such considerations are of importance also in local or spinal anæsthesia in which shock may be produced similarly from the hyperpnœa of an excited patient. Too often other possible causes are sought for.

More recently Dale and his co-workers have obtained evidence that a toxin such as histamine causes adrenaline to be secreted, such as would be expected from a compensation on the part of the vaso-motor centre which controls the suprarenals through the splanchnic nerves.

Some criticism is sometimes expressed by surgeons who are unable to find

visual evidence of the "lost blood" at the periphery. The dilatation must be considered of a very general nature, affecting muscles as well as viscera, and even in experimental shock, where the "lost blood" is certainly at the periphery, it is not visible, while the increased capillary permeability prevents engorgement.

In abdominal operations the mere handling of the intestine may cause the absorption of toxins from the lumen where they exist normally and their effects may be increased by acapnia. We know that even a partial strangulation of a hernia may cause death and here it would be well to emphasize the observations of Dale and Laidlaw that general anæsthesia increases enormously the effect of toxins which the body may be able to deal with normally. It would not indeed be too much to urge the use of local anæsthesia and narcosis in obstruction cases of any standing since we know how poor is the prognosis after a general anæsthetic.

General Considerations.—Whether the failure of the vaso-motor system be due to peripheral or central causes, the practical effect on the circulation is the same, namely, that there is an increased capacity of the vascular system and there is a diminished return of blood to the heart (oligæmia). Experimentally, the fall in venous pressure which occurs is very clear. There is, however, one point over which there has been some difficulty, namely, the actual state of the arteries in shock. It may now be stated that when the shock is due to capillary dilation as a result of toxins, the arteries are undoubtedly constricted, as has been emphasized by Malcolm. This has indeed been shown experimentally by the writer and may be taken as evidence of an attempt at compensation, such as we know occurs in hæmorrhage.

The Symptoms of Shock, from whatever cause, as would be expected, are those of hæmorrhage, pallor being always an outstanding feature as a result of reflex arterial constriction. They are, however, of considerable diagnostic importance where there has been internal hæmorrhage, such as intestinal or uterine. There may be some nausea with a sensation of shivering, and if the hæmorrhage continues there is increased respiration, which becomes an actual air-hunger, while the patient breaks out in a cold sweat. He is frequently restless, and there may be difficulty in keeping him in bed. In the more insidious toxic form the patient is more usually apathetic, the skin is cold, grey and clammy, sensory stimulation awakens little or no response, the limbs are limp and flaccid, the pupil is dilated and responds little, if at all, to light, the pulse is rapid and is felt with difficulty because of contraction of the artery. The respirations are rapid and the temperature is subnormal. The cold grey skin is the result of

constriction of the superficial vessels in their attempt to conserve the blood for the more important organs, especially the heart and brain. The difficulty of obtaining a response to sensory stimulation appears to be due to the fact that the conductivity through the synapses is much reduced by the low pressure, for, as has been shown by Porter, the ease with which the spinal reflexes can be elucidated depends on the blood pressure. The thirst complained of by the patient is the result of deficient secretion of the salivary glands, and is the natural call of the body for more fluid to add to the blood volume. The lowered body temperature results from the reduced metabolism.

The TREATMENT is indicated by the obvious attempt of Nature to keep up the blood pressure. The heart is seldom impaired in clinical cases. Whether the fall of blood pressure is due to the diminished volume, actual or relative, or due to diminished peripheral resistance, it is evident that Nature, as the thirst and cold skin indicate, is doing all she can to maintain the blood volume. This, then, is the essence of treatment. As much fluid as can be taken *by the mouth* is a primary physiological indication, and this refers also to the condition of fever in which excessive water is lost from the skin. More rapid effects are produced by intravenous saline injections of 0.9 per cent. sodium chloride, or approximately a teaspoonful of salt to a pint of boiled water. The saline, however, is not retained long in the vessels, having an appreciably lower osmotic pressure than the whole blood. The salt, too, is excreted by the kidney. In cholera, where excessive fluid is got rid of by the intestine, Rodgers introduced hypertonic saline treatment to assist in maintaining fluid in the blood-vessels as long as possible. The extra salt, however, rapidly attracts water and is not retained very long. Transfusion of blood may be used, but care must be taken that the donor belongs to the proper blood group (see page 129). Under conditions of emergency it may be necessary to have recourse to artificial fluids.

We owe to the work of Bayliss, Keith, and others, the provision of a physiological fluid, which in virtue of its osmotic pressure and colloidal nature is retained in the blood-vessels. They found that the addition of 6 per cent. of gum to the saline provides this requirement. Care must, however, be taken that the solution is neutralized. Erlanger and Gasser have further elaborated the suggestion of Bayliss. After a great deal of careful work in which the final recovery of the animal, rather than the immediate recovery of blood pressure, was the criterion of success, they have concluded that it is better to give the concentrated gum slowly, in order to attract fluid from the tissues. Solutions containing 25 per cent. of gum arabic, and 18 per cent. glucose, infused at the rate of 5 c.c. per kilo per hour, are recommended. This slow rate of in-

fusion is important with all gum solutions, especially strong ones, otherwise sudden death may result. Simultaneous records (in animals) of the arterial, pulmonary and venous pressures indicate that not only may rapid injection cause impairment of the heart, but there may be difficulty in getting it through the lungs. Neglect of this consideration and faulty preparation (as was inevitable under the hurried conditions of war-time) have done much to detract from the success of such an administration.

Acapnial shock is to be prevented rather than treated. Acapnia should be prevented by a sufficient depth of anæsthesia, and if necessary, supplementing the ether by morphia in an excitable patient. Henderson recommends the routine administration of carbon dioxide with anæsthetics, and this is now being used with success both in this country and in America. The addition of chloroform to ether undoubtedly lessens the stimulating action of the latter, and hence no doubt the comparative rareness of shock in Scotland.

Experimentally, the simplest method of preventing acapnia is to cause the animal to breathe through a long tube, and so increase its dead space; and in operations in which stimulation is specially liable to occur, there seems no reason why a similar procedure should not be resorted to by means of a closely-fitting face-piece to which a tube is attached, the anæsthetic being administered at its peripheral end.

Central failure of the vaso-motor centre of a more temporary nature occurs in fainting, in which a loss of consciousness occurs from cerebral anæmia. The centre may be unable to cope with an excessive dilatation of the skin, but in fainting due to emotion the centre appears to fail almost entirely (see "Consciousness"). This may no doubt in some instances be due to acapnia, as indicated above, but the suddenness of the onset suggests a more purely nervous cause in many instances.

The conception of the existence of a vaso-motor centre is as yet comparatively crude and depends in the main on the fact that if slices are cut off the brain, the blood pressure does not fall until the region of the medulla has been reached. It is, however, by no means clear that this is not simply an interference with the reflex arc through which pressor impulses are constantly being emitted as a result of afferent stimuli, nervous and chemical. Sudden fainting from an intense sensory stimulation, such as great pain in reduction of a dislocation, the incision of a whitlow, or seeing a disagreeable sight, emphasizes the reflex nature of vaso-motor tone. In such circumstances the higher centres apparently increase the normal inhibitory action over the lower reflex mechanisms, many of which we know to be disturbed under similar conditions of emotional stress.

That afferent impulses of a pressor nature are constantly being sent out is undoubted, and is evident from the experiment quoted above, or by isolation of the medulla from its lower nerve connections. There is also plenty of evidence to indicate that the tonic action of the so-called centre is increased as a result of certain procedures, such as sensory stimulation. All these are of a similar nature and indicate a primitive protective mechanism of the animal.

Blood Groups.—The transfusion of blood, however, is not by any means free from danger, even although actual infection is not transmitted from the donor to the recipient. In choosing a donor, his previous history has to be carefully investigated, particularly in relation to diseases of which he may be a carrier. All due care, also, has to be taken to prevent the transference of clots, the formation of which is commonly prevented in direct transfusion by means of a paraffined cannula or the addition of citrate to the blood after its withdrawal from the donor.

With all such precautions, however, it has been found that not infrequently patients may collapse after such transfusion. Since, of recent years, the danger of allowing a lowered blood pressure to be prolonged has been emphasized, it has become more important to consider more carefully the cause of such collapse. The discovery of Landsteiner in 1901 that the serum of one individual might cause agglutination or clumping of the red blood corpuscles of another, has given the key to the cause of such disasters, and it is now recognized that the blood of different individuals is divisible into four distinct groups according to their compatibility with each other. It has been thought that near relationship between two individuals might indicate that they belong to like groups, but Skinner has found that the blood of a child, although frequently of the same group as that of its mother, is often incompatible.

In determining the blood group to which an individual belongs it is necessary to have a sample of serum of groups 2 and 3. The unknown blood is mixed with the known sera in hanging drop preparations, as used in bacteriology. In ten minutes or so the agglutination, if present, is seen with the low power of the microscope, and is even visible to the naked eye. The differentiation is by this means easy. Group 1 (using Moss's classification) is agglutinated by both the known sera, but group 4 by neither. Group 2 corpuscles are agglutinated by 3 but not by 2, while group 3 is the reverse. For completeness it may be added that group 4 agglutinates all others, but its corpuscles are not agglutinated by any other serum, while group 1 is the reverse, i.e. it is agglutinated by all other groups, but agglutinates no other corpuscles. For this reason group 1 is known as the "universal recipient."

It will be obvious that an individual of a particular group cannot receive corpuscles from any donor whose cells it agglutinates.

For example, 4 cannot receive from 1, but as the converse is also true, 4 can always give to 1. These facts find expression in Landsteiner's Law, which states that there are always present in an individual blood agglutinins against the agglutinable substances absent from that blood.

In practice, then, an individual can only take from his own group or from one to which he cannot give, and can only give to his own groups or to one from which he cannot take.

Theoretically, the donor's serum might have the effect of agglutinating the recipient's corpuscles, but as the transferred serum becomes so diluted for practical purposes this can be neglected.

In choosing a donor, group 4 is the most generally useful, as he can give to all other groups. In an emergency it is of great advantage to know at once where such a so-called *universal donor* is to be found, as it avoids the necessity of determining the group of the recipient.

The importance of the blood groups is not, however, as emphasized by Swan, and by Dykes, confined to transfusion, as it is found that in skin grafting it is desirable to have the recipient and donor belonging to compatible blood groups, otherwise the grafts may not take. The importance of this fact in other varieties of grafts, such as ductless glands, is no doubt also true. In medico-legal work, too, it will be evident that the finding of the group to which an unknown blood belongs or does not belong may assist in the elucidation of a crime and it has been found possible to find the groups even with dry blood. It has been found, too, that if both parents chance to belong to the same group, their children belong either to that group or to that of the universal donor, i.e. group 4, a fact which might be of considerable value in questions of doubtful parentage.

THE NATURAL ARREST OF HÆMORRHAGE

The necessity for the arrest of hæmorrhage has received attention from early times, and is important to the surgeon, physician and obstetrician alike. Were it always possible to tie the injured vessel, the arrest of hæmorrhage would be a simple matter, but where this is not possible and, indeed, commonly it is not, the matter is much more serious and a knowledge of the physiological factors concerned in the normal arrest is desirable. These factors may be divided conveniently into two classes,—the power of closing the blood-vessels, and the coagulation of the blood.

Blood-Vessels.—An artery when cut, or even when punctured, at once contracts. This is well seen if a main artery be punctured for the purpose of withdrawing blood and it is rapidly realized by a young house surgeon assisting at his first operation. If the artery, however, when ruptured, even a large artery, be twisted or lacerated, the contraction of the vessel is increased and this prevents blood loss. Thus it is possible for an individual to have an arm torn off and yet not suffer from severe hæmorrhage. The blood loss itself, and the oxygen want caused thereby (as dealt with more fully in Chapter XX), act as a further arterial stimulant. The arrest is facilitated by the fall of pressure occasioned by the actual loss of blood. This, together with the other factors, is often sufficient to prevent death even from direct section of a large vessel, such as the radial artery.

Coagulation of the Blood.—Of recent years the general conception of the coagulation of the blood has shown definite signs of distinct simplification along physio-chemical lines and the conception of Pickering of this laboratory appears to be open to fewer objections than any other. According to this view, there exists in the blood a colloidal clotting complex (fibrinogen-prothrombin) which maintains its fluidity in virtue of its being associated with a protective substance. Clotting takes place if the protective substance be disturbed and the clotting complex split up as normally occurs when the blood comes in contact with any surface which it may wet.

The changes which take place are, we believe, the conversion of prothrombin into thrombin, with the assistance of calcium, and the subsequent action of the thrombin upon the fibrinogen, which is converted into the fibrin of the clot.

The exact nature of the substances just named is not yet certain and they have been identified rather by their action than their chemical composition. It may therefore be necessary later to subject this conception to some alteration when our knowledge of the physical chemistry of the proteins increases. It seems certain that the final explanation will be along such lines, and for the moment it explains all the facts of the coagulation of the blood.

Several features of blood-clotting are important clinically. It is known, for example, that the clotting of blood is hastened appreciably by heat and this finds expression in the clinical application of heat to wounds for the prevention of hæmorrhage on bruising or in the use of hot douches for post-partum hæmorrhage. The efficacy of the latter is generally accepted, but its action has more commonly been attributed to the effect on the uterine blood-vessels than on the coagulation of the blood. It has been noted, too, by Pickering that in some varieties of hæmophilia the delayed clotting is a matter of thermo-stability

and the application of heat to wounds of some hæmophilics will cause clotting in normal time, a fact probably not taken sufficient advantage of in practice.

It is clear that all cases of hæmophilia have not the same ætiology and there is considerable evidence to indicate that the condition should be considered a symptom rather than a disease.

The stasis of blood is also important in relation to blood-clotting, as not only does it allow the thrombin to act locally, but it permits the clot to become firmly adherent and block the ruptured blood-vessels. These facts are taken advantage of in the application of cotton-wool to a cut or of the plugging of a bleeding cavity temporarily, such as a wound in the skull, where other treatment may not be possible.

The later contraction of the clot, and its subsequent formation into fibrous tissue, completes the process of natural repair. Advantage of this is taken in the surgical treatment of aneurysm, where the inside wall of the aneurysmal sac is scarified or has passed into it a foreign body such as a silver wire. In the spontaneous cure of varicose veins, also, the question of stasis is important, and, indeed, may be of primary importance. The breaking off of a part of the clot and its subsequent carriage into the circulation may give rise to the formation of an embolus in a vital organ and cause death, as occurs not infrequently, when clots become detached from cardiac valves. Sufferers from inflamed varicose veins, especially where "knotting," i.e. clotting, has occurred, must be warned against use of the limb, since, as we have seen on page 92, muscular movement tends to drive the blood, together with the clot, along the blood-vessel in virtue of the valves in the veins.

CHAPTER XVI

THE HISTOLOGY OF THE BLOOD

Microscopical examination of the blood is now almost a routine procedure in clinical work. Its histological examination is divided into a quantitative and qualitative study of its cellular elements, and a search for abnormal constituents, such as parasites. The reader is referred, for details of the methods, to the many excellent manuals of clinical and laboratory work.

The Red Blood Corpuscles.—These cells are normally present in the blood to the extent of about five to six million per cubic millimetre. They contain the hæmoglobin upon which depends the oxygen-carrying power of the blood. It is quite amazing the extent to which the number of red cells may be diminished during life. In pernicious anæmia, for example, they may be reduced to 600,000. The general condition of the patient, provided he is resting, is often quite good on account of the adaptation of the circulation, although any exercise will be impossible.

In disease the development of the blood is of great interest, for if the red cells are being destroyed too rapidly or have been lost by hæmorrhage, immature forms may find their way into the circulation and there be recognized. In adult life the blood is chiefly produced in the red marrow of the short and irregular bones. In time of stress the yellow marrow of the long bones may be called into use. The adult red cell is the erythrocyte, a non-nucleated cell with an average diameter of 7.5 μ or between 7 and 8 thousandths of a millimetre. In disease many other forms may appear, of varying size and shape. Of recent years cultures of bone marrow have shown that what appeared to be erythrocytes may arise as buds from more primitive forms, not necessarily from nucleated cells by the loss of the nucleus, as has been generally considered. The essential stimulus to corpuscle formation and extrusion appears to be oxygen want, which has been dealt with in the chapter on "Anoxæmia." Though oxygen want may lead to an increase in the total number of red corpuscles, yet in some circumstances it does not lead to the appearance of primitive forms in the circulation unless associated with a reduction in the number of normal forms, either from actual loss, abnormal destruction, or a deficiency in the mechanisms producing

them. Thus in circulatory disease there may be an increase in red cells, but there are no abnormal forms, as in the anæmias.

Nucleated red cells and cells with reticulæ which can be shown up with a special stain, and abnormally large or small erythrocytes occur in the milder anæmias. In the severer forms, such as pernicious anæmia or the anæmias brought about by intestinal worms (as in ankylostomiasis), the common parasite of the tin mines, large nucleated reds known as megaloblasts, or distorted forms (poikylocytes), make their appearance and have thus a special diagnostic significance, and may be the first indication of the presence of parasites. It is interesting to note that in the case of the secondary anæmias the red blood corpuscles contain less than the normal amount of hæmoglobin. This we know because the colour produced by a given number of corpuscles is less than that which would be given by a similar number of normal ones. That is, the colour index is low. In pernicious anæmia, on the other hand, where although the corpuscles are abnormal they each contain an abnormally large amount of hæmoglobin, the total amount of hæmoglobin in the body may be appreciably reduced in virtue of the small number of corpuscles.

The red blood corpuscles are apparently being constantly removed, and the hæmoglobin broken down in the formation of bile (see page 253). The disintegration appears to take place in the spleen, hæmolymph glands, even in the blood itself, and possibly the liver, where at least the disintegrated corpuscles find their way. Whether or not any abnormality in the breaking-down of corpuscles may be significant of disease is unknown. It is of interest that recently Barcroft has brought forward evidence to indicate that apparently reserves of red blood corpuscles may be held in the spleen from which they may be extruded and made use of in an emergency.

The White Blood Corpuscles.—The white blood corpuscles have all the appearance of being active living cells which act as the scavengers of the body and protect it from bacterial injury. The method by which they are attracted to the spot of injury or invasion is as yet unknown, although the term chemiotaxis is generally adopted to suggest that the stimulus is probably a chemical one. The leucocytes can wander in and out of the blood-vessels, while the polymorphonuclear cells have a special property of investing and destroying bacteria or other dead matter, the so-called power of phagocytosis. Leucocytes are differentiated according to their histological characteristics, as shown by stains. Polymorphonuclear cells (70 per cent.) are largest in number and are so called because of their finely granular lobular nucleus which varies in shape. Their phagocytic power is specially facilitated by their being possessed

of amœboid movement. If they stain with neutral dyes they are known as neutrophils, but if they stain with basic dyes, such as methylene blue, they are known as basophils, a variety which occurs in the blood normally to an extent of less than 1 per cent. A more common form is the coarsely granular eosinophil, so called because it stains with acid dyes such as eosin.

The lymphocytes are distinguished by their having a large round nucleus almost as large as the corpuscle itself, which is otherwise hyaline and colourless. They are of two varieties, large and small, and are found normally in the blood to form 25 per cent. of the total white corpuscular count.

Normally the relative number of each group is fairly constant, but in disease the proportion may be much changed and investigation to determine this proportion, the so-called differential count, is of considerable clinical value. In acute conditions the polymorphs are increased, while in more chronic states, such as tuberculosis, the small lymphocytes specially predominate. For reasons as yet unexplained eosinophilia is often associated with the presence of parasites, e.g. ankylostomiasis, and is found sometimes in asthma. An abnormal number of large lymphocytes commonly occurs in malaria and other protozal diseases which suggests that these cells have a special protective power in relation to such parasites.

The total number of white corpuscles is by no means so constant as that of the red corpuscles, and may vary in health between 8,000 and 15,000 per centimetre. In old age the number tends to diminish. A variety of conditions, even the taking of food, a cold bath, or exercise, brings about normally a leucocytosis, as does also the administration of certain drugs, such as potassium chlorate, thyroid extract, and essential oils. The absence of a leucocytosis, which is an indication that the body is not responding properly, is an omen of grave insignificance in acute disease. In special instances, such as typhoid fever, influenza, acute miliary tuberculosis, it may assist the diagnosis, as in these conditions a leucopænia or diminution in the number of leucocytes is fairly frequent. The presence of a polymorpho-leucocytosis in conditions where this is not normally present, e.g. tuberculosis, is often of value in causing suspicion of some complication.

It has been found by Widal and emphasized by Wilson that the absence of a post-prandial leucocytosis is indicative of liver impairment, as it was considered that this organ could prevent the entrance of substances, especially proteins, into the general circulation. Blood examination, as a test for liver efficiency, is made before and after taking seven ounces of milk instead of breakfast.

Of considerable interest is the *development of the white blood corpuscle,* as in disease more primitive forms than that found normally may be thrown into circulation. Some little difference of opinion exists regarding the details, but the bulk of evidence indicates, according to Muir, that all the leucocytes of the myeloid series are derived from primitive non-granular cells or myeloblasts which have a large single nucleus closely resembling the progenitor of the lymphocytes. The myeloid series include the polymorphs and the more coarsely granular eosinophils, basophils, and neutrophil polymorphs. This series may be looked upon as being derived from bone marrow as the result of myeloblastic reaction. The lymphoid series, which include the small and large lymphocytes, come from lymphoid tissue scattered throughout the body, e.g. lymph glands, tonsils, Peyer's patches, and splenic corpuscles. In these glands lymphocyte formation may be seen. Normally the myelocytes do not leave the bone marrow. In diseased conditions where the leucocyte-forming tissue appears to proliferate, they may be thrown into the circulation. More especially is this so in myelogenous or spleno-medullary leukæmia, and occasionally in hæmorrhage, in which the number of leucocytes (particularly the polymorphonuclear cells and myelocytes) present in the circulation may be over 300,000 per cubic millimetre. In the lymphatic leukæmias, on the other hand, there is an enormous increase in the lymphocytes, either variety predominating. In all forms a certain amount of anæmia is also present, and also enlargement of the spleen. This latter condition is very prominent in the spleno-medullary variety.

CHAPTER XVII

PHYSIOLOGICAL PRINCIPLES IN RELATION TO CARDIAC EFFICIENCY AND DISEASE

The physiological aspect of cardiology has been very prominent of recent years, largely owing to the work of Mackenzie, Lewis, Starling, and their pupils. Attention has been particularly focussed on the musculature of the heart. While the state of the valves may, if diseased, be a valuable aid in diagnosis and prognosis, yet it is the power of the muscle to maintain the circulation in spite of the valvular defect, which is the real indication of cardiac efficiency, and which determines the capability of the patient in regard to exercise. Often, the absence of any obvious valvular disease leads to neglect of a condition of the musculature, which is just as dangerous and important.

Normally, the heart has to deal not only with the blood which reaches it during rest, but also with the greatly increased amount brought to it in exercise.

A heart may be efficient for its resting load, but quite incapable of doing any more work, either in the form of an increased blood-flow from the veins, or an increased resistance to its output. In such a case the muscle is exhausted, indeed some of its fibres may be destroyed by increased intra-cardial tension, or weakened by chemical poisons or the toxins of disease. The most striking example of the latter is seen in diphtheria, in which a patient has been known to fall back dead from cardiac failure on attempting to sit up. Hence diphtheria cases are kept strictly in the recumbent position for several weeks as a routine, for it is quite impossible from the local nature of the lesion to estimate the degree of impairment of the heart. The same applies to all forms of myocarditis and toxæmia, and herein lies the danger of a too vigorous examination of a case of acute pneumonia. In fatty degeneration and infiltration of the heart a similar state of affairs exists, except that in this instance the heart is impaired by the presence of fat, and the muscle fibres have been partly replaced by it. In toxæmic cases there is also often superadded the effect of the toxins on the peripheral vessels.

This power of the normal heart to respond to increased demands depends on two facts, namely, that it can increase its rate, and, at the same time, its output per beat. The mechanism whereby the rate is increased has been dealt

with. It is obvious that the faster the rate the less is the margin of reserve, so far as rate is concerned. Although an increase in rate may deal with the load of the nature of an increased inflow, what is just as important is load in the form of increased resistance due to contraction of the peripheral vessels, or breakdown in a valve. In exercise (see page 92) is added the load of increased inflow. So far as the heart is concerned the effect of both loads is the same. It can be readily shown experimentally that, if the resistance to the circulation is increased within physiological limits, the output of the heart is not affected except for a few beats. The small quantity of blood not expelled is added to the inflowing blood and the cardiac musculature is stretched so that the heart beats more forcibly and overcomes the increased resistance. Similarly, an increased inflow by filling the heart more fully during diastole causes the heart to beat more forcibly. This phenomenon has been called by Starling the "Law of the Heart." It states that the contractile power varies with the length of the fibres. Such a law, however, is one that may be applied to all muscular tissue, since all muscle contracts more forcibly when stretched.

The capacity of the heart, to which there must obviously be a limit, to deal with a load, is known as the *cardiac reserve*, or its power of compensation. On it not only depends primarily the power of the circulation to adapt itself to the increased requirements of exercise, but, if the reserve is small, the capacity of the individual to lead a reasonably normal life. Clinically, therefore, it is important to obtain some idea of the cardiac reserve in the patient. To obtain this he must be given some exercise to do, such as bending, hopping, lifting dumb-bells, or stepping on and off a stool. In all such tests the normal habits of the individual must be considered. For example, the lifting of 20-lb. dumb-bells every two seconds for half a minute does not represent much work to a stevedore, yet may be a considerable amount for a clerk. Notice should also be taken of any general distress shown by the patient, especially breathlessness. The pulse rate, especially the time taken to return to normal after exercise, is also of value. The physiological value of this observation lies in the fact that the less efficient the heart the more will the blood be banked up on the venous side and the longer will be the time required to get rid of this venous accumulation which increases the rate of the heart. It is considered that if one bends down twelve times to touch the toes as nearly as possible, the pulse rate should return to normal in half a minute. If it should not have returned in two minutes the heart is almost certainly seriously impaired. These tests are somewhat rough, as even such bending may represent a considerable amount of work to a stout individual. A variety of exercises should, therefore, be used before

arriving at an opinion. It seems doubtful if the effects of the administration of atropine have been sufficiently investigated as an estimation of cardiac reserve, since there is evidence that vagus tone is closely associated with the power of the heart to adapt itself to the increased venous pressure by exercise.

The effect of the exercise, especially if sudden, is greatly to increase the load on the heart and if the muscle is in such a state that it cannot deal with this increase two things must happen: the heart may cease to beat and the individual die at once, or it may dilate and partly evacuate its contents in the reverse direction into the veins instead of the arteries. The dilatation brings about a valvular incompetence due to disparative size or relative insufficiency and this may be looked upon as a safety-valve action. The valve, however, is only temporary, as it obviously throws an additional strain on the chamber behind. In the event of the left ventricle dilating there is an increased resistance in the pulmonary circulation, and the right ventricle has to do more work and, as it were, share the burden of what may be disease of the aortic valve. It is important to remember that the pressure in the left ventricle during systole is normally about 40–50 times that in the left auricle. A leak through the mitral valve, although it may have no effect on the arterial pressure, may bring about changes in left auricular pressure amounting to over 200 per cent. That such a condition may produce severe pulmonary symptoms is then not surprising. When, however, it is the tricuspid valve which becomes enlarged, the extra strain is placed on the right auricle and there is a marked rise in venous pressure with interruption of the venous return to the heart. Such a patient is considered to be a case of acute heart failure and should the load be increased beyond the limit of the safety-valve action, the heart, for reasons which will be seen below, may cease to beat. Even if this does not happen, the venous stasis gives rise to all the signs and symptoms of venous engorgement and slowly becomes incompatible with any form of activity, although unfortunately and not infrequently the earlier results are neglected by the patient. Whether the heart will cease beating or dilate depends on the state of its musculature and the size of the pericardium, which is primarily designed to prevent sudden stretching.

Function of the Pericardium.—The pericardium is essentially a fibrous sac with all the characteristics of fibrous tissue such as we are familiar with in other parts of the body. Such tissue does not yield to a sudden stretching, but may elongate to prolonged strain without rupture, provided the strain is not excessive. Hence its value in tendons, which do not stretch on rapid muscular contraction, though they may become longer as the result of the growth of bone. This feature is realized by the surgeon in the treatment of a torn

ligamentum patellæ, and the formation of scar tissue. The use of the pericardium is also well seen in athletes. Here the load put on the heart is often sudden and excessive. Such individuals often present all the features of acute cardiac failure, though none is present. The enormous rise in venous pressure is evident by the distension of the veins and the blueness of the cyanosis, as after a boat race. But for the pericardium this high venous pressure would distend the heart during diastole and the heart might be filled with more blood than it could deal with. The size of the pericardium is such that it does not allow the heart to be filled with more blood than the muscle can evacuate, even in severe exercise. In training for such exercise the cardiac reserve increases in order to deal with the increased blood-flow and resistance.

The above statement does not mean that athletes have enlarged hearts, as is sometimes imagined. The heart of an athlete at rest is not necessarily larger than that of an untrained man, but in exertion the trained heart may enlarge considerably without becoming inefficient, otherwise it would be impossible to have the enormous increase in the cardiac output not only per minute but per beat, which we know occurs. (A. V. Hill.)

The special properties of fibrous tissue are of extreme importance as they allow the cardiac muscle to hypertrophy and increase in size and yet retain its power of resisting any sudden stretching. It is this property, too, which is taken advantage of when the heart dilates as the result of excessive load. Here we see the difference, however, between what might be called physiological dilatation of the pericardium and that due to disease. If the pressure in the ventricle is frequently above normal the muscle hypertrophies in an attempt to deal with the increased content of blood and the increased tension causes the pericardium to be stretched. The hypertrophy, however, may not necessarily keep pace with the increased load placed on the heart, and the increased ventricular pressure continues the dilatation, as we have seen above. There comes a point, then, when, perhaps the heart, and in particular the pericardium, have not dilated sufficiently to permit all the safety-valve incompetence of the auriculo-ventricular valve. Moreover, the heart cavities may be filled with more blood than the muscle is able to deal with. The pericardium prevents further dilatation. If now a load is suddenly applied, complete heart failure will result, the ventricle failing to drive out its contents. The larger the heart cavity the less is the mechanical advantage at which the cardiac musculature works. Normally, the pericardium maintains the size of the heart, so that its muscle can act at the best mechanical advantage. When it is dilated it is evident that mere increase in the size of its cavities will further increase the mechanical load.

It is such danger of sudden death which has caused it to be averred that digitalis should not be given in disease of the aortic valve unless the mitral valve is incompetent to act as a safety valve. This drug by prolonging the diastole might so increase the filling to a dangerous extent, but as it at the same time increases its force of the heart the danger is minimized.

Acute Heart Failure.—The COMMON SYMPTOMS are: breathlessness, palpitation, sometimes cardiac pain, cyanosis, and venous distension, with, possibly, a venous pulse, which latter is more evident in the severer cases.

At first sight it might be expected that acute heart failure should be associated with a lowered arterial pressure. This is not necessarily the case, for a fall in blood pressure due to diminished cardiac output is prevented by bringing into action all the reflex mechanisms which are utilized in hæmorrhage (see page 122). There is, for example, reflex arterial constriction, and this is responsible, no doubt, for the pallor associated with cyanosis in cardiac cases. The engorged veins and venules stand out on a pale background. A falling blood pressure in a cardiac case must be looked upon as an omen of the gravest import.

The palpitation in heart failure is due to its excessive rate, brought about, as in exercise, by distension of the right auricle. The breathlessness is due to a variety of causes.

If, as in cardiac disease, there is a chronic leak backward into the veins, more acute symptoms, such as breathlessness, may disappear from relief of the pulmonary circulation, or possibly from exhaustion of the nerve endings concerned. The signs and symptoms of increased venous pressure continue, such as enlargement of the liver and œdema, while many organs may cease to function properly, such as the kidney and stomach. Unfortunately, the passing away of the more acute symptoms often makes such cases difficult to manage, as they do not appreciate the significance of the more chronic signs, such as œdema, although the latter may, as explained on page 279, persist for purely local reasons.

The TREATMENT of acute heart failure, apart from drug therapy, which really is subsidiary, is to reduce the amount of work done by the heart to a minimum. The patient is, of course, to be kept in bed and to be propped up, at first. This latter procedure is found to add appreciably to his comfort, and reduce the work of the heart by reducing the venous pressure. Also, by facilitating the descent of the diaphragm, it gives maximum aeration of the blood.

During the last generation there has been a fashion against the blood-letting which was so common in former days. Its value has been deprecated on the ground that the arterial blood pressure so very rapidly recovered that the

blood withdrawal was of no value. This passing out of fashion is based on an incomplete knowledge of facts. Although the arterial pressure rapidly recovers, this is mostly due to arterial constriction, but the venous pressure, which also falls, recovers comparatively slowly, as is readily shown experimentally. There may be no diminution in the resistance to the cardiac output, but there can be no doubt that a very large measure of relief must result from the venous fall since the heart is thereby given less blood to force out per beat. The greater use of blood-letting in properly chosen cardiac cases (which have an obviously raised venous pressure) is certainly indicated on physiological grounds.

As we have stated, however, as soon as the acute symptoms have passed off, it may be a little difficult for the patient to realize that his movements must still be limited. It may well be made a rule throughout the treatment of cardiac disease in all its stages that the patient should be allowed to do just a little less exercise than will bring about the symptoms of distress mentioned above. For example, he should stop short as soon as he becomes breathless, for any heroic attempt to prolong the exercise would only lead to further impairment due to the strain. So long as there is any indication that the cardiac condition may become worse or there is any œdema, every effort must be made to assist the circulation in the affected parts, and this can only be satisfactorily accomplished by keeping the patient in bed. Since the œdema is due to local anoxæmia and toxæmia, which results from back pressure in the veins, what has been written in regard to blood-letting applies here also, and such treatment must obviously be of value.

With regard to later treatment one must realize that it is just as bad for the individual to take too little exercise as to take too much. The heart has to compensate for the additional strain thrown on it by increasing the amount and efficiency of its muscle, but, by exercise, this margin of compensation can be appreciably increased. Any increase protects the individual against any strain which may be suddenly thrust upon him in an emergency and normally we have a considerable degree of cardiac reserve for this purpose. Mental states, such as anxiety, and excitement, should be avoided, for they increase the work of the heart and may be generally detrimental to the general well-being of the body, upon which depends adequate hypertrophy. Similarly, in considering the exercise, due attention has to be paid to the previous habits of the individual, as that to which he is accustomed is less liable to cause strain than a new form. Graduated exercises, provided they are done under supervision, give the patient a certain physical aim and some Spas, such as Nauheim, have specially graduated walks set out for this purpose. They give the individual something to do and this is in itself of importance as otherwise he is apt to become an invalid

and introspective when often there is no necessity whatever. At the same time the individual has to remember that he can no longer live a careless life and every effort has to be made to make him lead as simple and as physiological a life as possible.

Drug therapy concerns mostly the more acute cases and here the digitalis series is invaluable. By its use the heart is slowed and the conductivity of the auriculo-ventricular bundle is reduced. Hence it diminishes the number of impulses which can pass down from auricle to ventricle. Subsequently, as is to be expected, the effect of the drug is best seen when the ventricle is receiving an excessive number of impulses from the auricle as in fibrillation or flutter. The reduction of the number of impulses prevents the heart from having to contract too rapidly, too frequently, or at irregular intervals and hence it becomes more efficient as a pump. Obviously digitalis has to be avoided in a condition of heart-block in which the conductivity of the bundle is already below normal and which may be converted from a partial heart-block into a complete heart-block. It is also possible to reduce the rate of the heart to an excessive degree and it may be taken as a rule that the drug should not be administered when the pulse rate is under 80 per minute.

There is often so much anxiety and fear of impending death on the part of the patient that small doses of morphia may be necessary, as the mental state itself tends to disorder the cardiac mechanism. An eighth of a grain of morphia, with a one hundredth of digitalin or strophanthin, are commonly administered in such an emergency. In this relation hypodermic or intravenous medication is often desirable where there is reason to believe that secondary to the heart condition there is impairment of intestinal absorption as the result of venous congestion.

The administration of drugs of the alcohol series is an interesting speculation much adhered to by the older physicians. Until lately it was considered that, apart from the sense of confidence given to patients and possibly a little reflex stimulation, they are of little avail. More recently, it has been shown by the writer that alcohol causes a profound fall of venous pressure which will, if brought about in man, be of considerable relief to the heart. The action of the alcohol is analogous to the effect of blood-letting, which noticeably reduces venous pressure (see page 123). If the letting is continued—it will actually reduce arterial pressure (say 30 ounces)—we may presume the venous pressure has been very much reduced.

The reputation of strychnine in cases of circulatory failure requires some remark, since of recent years the fact that the drug has little effect in the iso-

lated heart has rather led to its disuse. Hale White, on the other hand, goes so far as to say that "patients almost dead from failure of the heart in the course of chronic cardiac disease may sometimes be brought round by a subcutaneous injection of strychnine." This is undoubtedly due to the effect of the drug on the vaso-motor reflexes which are brought into operation in the maintenance of aortic pressure when the cardiac output is reduced. We know that the cardiac contractions depend to a very appreciable extent on the aortic pressure which they maintain. When there is then a mutual failure the strychnine may just suffice to break the vicious circle.

CHAPTER XVIII

BREATHING

Breathing, in its broad sense, is the movement made by the body to maintain pulmonary ventilation. As such it may be considered the external expression of the body for the need of oxygen and the removal of carbon dioxide, which are essential for the maintenance of the full function of any tissue. In order that the tissue may be thus provided, the blood must be capable of performing this double function in accordance with the needs of the tissue which may vary enormously according to their activity. To ensure this, the oxygen and carbon dioxide must be maintained at a constant level and provision made for varying requirements. Now the effect of increased tissue activity is to increase the demand for oxygen for oxidation and cause a greater production of carbon dioxide, and if these gases are to be maintained at a constant level in the blood, there must be better loading of oxygen and unloading of carbon dioxide in the lungs. This is brought about by variations of breathing and must be delicately adjusted to the requirements of the tissues. It is brought about by the activity of the respiratory centre. (Although the term "respiratory centre" is used; in view of the fact that the recent work of Lumsden indicates that respiration depends on a much less localized area than used to be imagined, it would perhaps be more accurate to use the plural.) The respiratory centres, which lie in the pons and medulla, act as a gauge of the carbon dioxide and as such are much more delicate than any instrument known to science.

Should the gas increase, the respiratory centre is stimulated, the breathing increased, and the extra carbon dioxide is got rid of. In the same way a fall of carbon dioxide in the blood causes a cessation of respiration. Excess of carbon dioxide appears to be more important as a stimulant of the respiratory centre than lack of oxygen. The latter, however, has been shown to be effective in varying the sensitiveness of the centre to carbon dioxide, possibly by facilitating the production of lactic acid in the centre itself. In actual fact, except in pathological states and rare conditions which cannot be considered possible in the life of the primitive animal, deficiency in oxygen and excess of carbon dioxide, occur together and even if the centre reacts only to carbon dioxide, the supply of oxygen is safeguarded. At rest, and still more in sleep, the

oxygen required is small, the carbon dioxide produced but little, and the breathing so slight as to be imperceptible to the individual. The more active he is the greater is the requirement of oxygen and the greater the tendency for carbon dioxide to accumulate in the blood and cause a corresponding increase in breathing. At the end of severe exercise breathing will be very laboured. This may be considered physiological dyspnœa or breathlessness in which he is attempting to get rid of the extra carbon dioxide which has been produced during the exercise. We shall see, however, that the body may get rid of carbon dioxide in anticipation of exercise or may utilize the excretion of carbon dioxide by the lungs as a method of removing acid from the body. In each instance this getting rid of carbon dioxide is characterized by breathlessness.

To understand breathing thoroughly we must realize what is happening in the lungs. There the blood is, as it were, spread out on an enormous surface where it is exposed to the alveolar air with which it rapidly gets into gaseous equilibrium through the walls of the blood-vessels, which are extremely thin, the same cells acting as a wall to the capillary and to the alveoli.

Such a large surface in the body can only be secured by the anatomical arrangement existing in the lung which is comparable to the enormous surface exhibited by a tree with leaves which, indeed, are developed for a similar purpose. But the anatomical arrangement does not permit of mixture of the alveolar air and outside air at a speed sufficient to maintain the requirement of the blood if that mixture is dependent on diffusion alone. This can only be done by mechanically replacing a large amount of air in the respiratory tract by the process we know as breathing.

The act of breathing, then, depends on a large number of factors, all of which are important to the clinician. When a breakdown occurs there is an attempt on the part of the other factors to make up for the deficiency.

The factors which are now dealt with in some detail are the respiratory centre, the respiratory surface, the replacement of the respiratory air, the pulmonary circulation, the cerebral circulation, the blood, the quality of the air breathed and all those organs which assist in maintaining the neutrality of the blood.

The Respiratory Centre.—We have already seen that the gaseous content of the blood is the main determining factor in the activity of the respiratory centre. This matter is dealt with further below under "Cerebral Circulation." Certain other mechanisms of a nervous nature have also an important influence, either by varying the sensitiveness of the centre or by direct nervous action. The object of these mechanisms appears to be twofold: (1) to give the body a

greater range of activity; (2) to increase the respirations prior to contemplated or expected activity. The former is exemplified by the action of the vagus when the lungs are stretched. When the lungs are expanded to a certain extent in inspiration an impulse passes up the vagus which results in the inhibition of inspiration and the commencement of expiration; an impulse with the opposite influence passes up the vagus when expiration has proceeded to a certain extent. Respiration is thereby prevented from being excessive and no doubt this vagus action is important in maintaining the reserve respiratory surface necessary for increased activity. In the chapter on "Exercise" it will be seen that such mechanisms are of common occurrence in the body and particularly in respect to circulation have we observed the benefit of vagus tone. This reflex, known as the Hering-Breuer reflex, may become unduly exaggerated in clinical conditions, and this appears to be partly the cause of the rapid shallow breathing in some cases of cardiac disease, pneumonia, pneumothorax and possibly also in pleurisy. In the two latter conditions the rapid shallow breathing may be brought about by the knowledge of the patient that deeper respiration is liable to cause intense pain.

There is some doubt as to the mechanism of the production of shallow breathing. It may be the result of effects on the respiratory centre and this is suggested by experiments which tend to exhaust the centre. On the other hand, the fact that it is obtained after inhalation of irritant gases or in nervous conditions such as neurasthenia, shock and hysteria, in which there is great exaggeration of reflexes generally, indicates that the shallow breathing may be a simple exaggeration of a normal reflex. That in pneumonia the shallow breathing is not due to the toxin is seen by the fact that in pneumococcal conditions in other regions such breathing is not seen. Irritation of the thoracic fibres of the vagus or increased sensitivity of the nerve endings leading to exaggeration of the Hering-Breuer reflex seems then to be the most important cause.

In the second category we may place stimulation of the respiratory centre by higher centres. It is well known that the emotions frequently cause great increases in respiration. The respiration mechanism is as it were anticipatory, and we have seen that there is a similar increased activity on the part of the heart. Fear of news which the physician may impart is often a sufficient stimulus, and the practitioner knows that if he desires to count the respirations it is desirable to hide his intention.

The increased respiration which occurs on stimulation of sensory nerves is no doubt of similar nature and part of a primitive defensive mechanism by

which the animal is at once made ready for increased activity. As the results of the increased breathing the carbon dioxide is washed out and immediate respiration is not essential. This may be imitated in voluntary forced breathing, after which there is a period of apnœa. Such a period will obviously be of immense value in a sudden emergency as more time will be available before the accumulation of carbon dioxide renders respiration imperative. In this respect it must be remembered that in muscle work the accumulation of carbon dioxide is more important than oxygen supply which, although necessary in the recovery process, may not be absolutely essential for muscle contraction. Indeed an oxygen debt may be established. Stimulation of respiration may be brought about by stimulation of any sensory nerve: slapping with a towel, rubbing the chest or face, pulling out the tongue, are all methods in frequent use by the anæsthetist and accoucheur when breathing is not so good as desired. In operations on the breast, such as the removal of a carcinoma, the effect of such stimulation may be very marked, and care must be taken that the patient does not get an overdose of the anæsthetic as a result.

The breathlessness of some cardiac cases may be due to a similar sensory stimulation within the pulmonary circulation (*q.v.*).

The temperature of the blood has now been shown to increase the sensitivity of the respiratory centre. Haldane found that it is even possible to be so stimulated that the body has an excess of carbon dioxide, and in order to maintain the body neutrality there is an increased alkali excretion by the kidneys. This will be of value in exercise, and in pyrexia the quickened respiration may be partially caused thereby.

While stimulation of the respiratory centre is perhaps of the greater interest to the physiologist, to the clinician diminution in the activities of the centre is of serious importance. Failure of the respiratory centre is a common cause of death, as has been indicated in Chapter I, but not only is it a cause of sudden death, it is also a method by which the fatal termination is brought about in many chronic conditions. Failure of the respiration in such conditions occurs by exhaustion of the centre or the loss of neutrality of the blood. Failure is also caused by the extension upwards of spinal disease or downwards of cerebral disease, and also by increased cranial pressure. Clinically, failure as the result of the action of poisons is fairly often seen. Opium, anæsthetics and alcohol are well known to cause death in this way, and the principle of treatment in emergencies will be indicated later. Such failure is the common termination of nervous diseases, whether acute or chronic, as the degeneration slowly affects the centre. In such cases the mentality may be good, depending

on the nature of the condition, until a few minutes before death. In cases such as bulbar paralysis or ascending sclerosis many normal functions have already been lost and death is a merciful release from a pitiful existence, as these cases, though prolonged, are hopeless from the first. Fortunately many are carried away by inter-current disease at an early stage.

The centre may also fail, as emphasized by Yandell Henderson and his co-workers, from an excessive loss of carbon dioxide (acapnia) and this is specially liable to occur during anæsthesia. In the first instance there is an excessive stimulation of the centre due to the operative procedures—especially if the anæsthesia is light. There results a washing-out of carbon dioxide from the body and a stage is reached when there is insufficient to stimulate the centre, which is already depressed by the anæsthetic. Death ensues from oxygen want unless respiration can be made to recommence by the administration of carbon dioxide and sensory stimulation. A less severe acapnia may result in a variety of surgical shock, as tone of the vaso-motor centre is also dependent on the carbon dioxide content of the blood.

The partial failure of the respiratory centre may be the result of exhaustion. Such fatigue is seen if respiration is obstructed. If the experiment is carried out in a human being it is seen that the respiratory centre makes an effort to cope with the obstruction, but as carbon dioxide accumulates it eventually breaks down and the respirations become rapid and shallow—a type of breathing that is of little real respiratory value. This point is to be borne in mind in the construction of respiratory apparatus, such as gas masks and divers' apparatus, and in order to prevent the possibility of such obstruction the diameter of all respiratory tubes must be at least one inch. It is considered that this fatigue may be largely the cause of the rapid and shallow breathing seen frequently and discussed above. The more fatigued the respiratory centre the more appears to be the power of the Hering-Breuer reflex and similar symptoms are seen when the reflexes are exaggerated.

A more chronic form of fatigue may be brought about in conditions such as adenoids, with the result that the carbon dioxide finds its exit by channels other than by the respiration; as the result, however, of the diminished breathing a very chronic form of anoxæmia is sometimes seen.

In judicial hanging death is really due to failure of the respiratory centre to transmit impulses to the muscles of respiration because of the destruction of the spinal cord, shock rendering the individual immediately unconscious.

Respiratory Surface.—In giving a general conception of the nature of respiration in the lung, it has been seen that a minimum surface is necessary,

together with additional surface to spare, for any increased activity. Actually the internal surface of the lung is much beyond the requirements of the resting organism. One lung would supply sufficient oxygen and remove the necessary carbon dioxide. This is readily seen experimentally, or in pleurisy with effusion, and is even taken advantage of in the treatment of pulmonary tuberculosis, where one lung is put at rest by an artificial pneumothorax. Normally, a large amount of both lungs is not being used. The extra surface is available in exercise and is used in deep breathing. By increasing the rapidity with which the air in the respiratory tract is changed, aeration of the blood is further benefited. The surface available depends on the individual development of the chest. The simple measurement of its circumference at its widest part gives to the clinician an indication of the amount of respiratory surface, provided there is nothing pathological in the lungs themselves. The normal circumference is considered to be from 34 inches in expiration, to 37 in inspiration. The difference between these measurements gives some indication of the spare surface available but probably only a small part of it, since in men diaphragmatic breathing is so important. It is, however, an indication of the vital capacity, which, as we shall see below, is of very considerable importance.

Certain parts of the lung are normally less used than others, and we know that these parts are very liable to become the seat of tuberculous disease, such as the apices and roots. Limitations of expansion indicate deficiency in the spare surface, but this is not necessarily to be seen in the depth of respiration. Thus if one part of the lung is prevented from expanding and normal chest movements occur, the other parts will expand to fill up the space made by the chest on inspiration. In this way we have what is known as compensatory emphysema. Clinically, the finding of such patchy emphysema is often of diagnostic value, as it may indicate local lack of expansion elsewhere, e.g. deep pneumonia or pressure on the lung.

Diminution in the surface is a common clinical condition and may be brought about by affections leading to pressure from without or interference with the surface from within. A typical instance of pressure from without is seen in pleurisy with effusion, empyema or hydrothorax. In these conditions the residual air, i.e. the 500 c.c. which cannot normally be forced out of the lung, is slowly driven out and the lung collapses. All conditions such as neoplasm will, of course, have the same effect, and although the pressure, e.g. of fluid, may be removed, the lung does not necessarily expand at once, as it may be prevented from doing so by thickening of the pleura, the result of the inflammatory condition. The withdrawal of the fluid may then so increase the

negative pressure on the chest that disastrous effects such as acute dilatation of the heart and displacement of the organs to the side of lesser pressure may occur. This is guarded against by abstaining from removing too large a quantity of fluid at a time.

A similar condition of lung collapse is brought about when the negative pressure disappears, as in pneumothorax or injury when air gets into the pleural cavity, but fortunately such conditions are usually unilateral and the wound becomes closed off by adhesions between the visceral and parietal pleura, while the air is rapidly absorbed.

Diminution of surface from internal causes in the lung is common. Should, for example, a bronchus or a bronchial tube be blocked (a fairly common condition in bronchitis and pneumonia in children), the air in the peripheral alveoli rapidly becomes absorbed and collapse of the lung ensues. There is then marked reduction of surface. The symptoms of this collapse are essentially different. In the first instance they are referable to the interference with the replacement of the alveolar air, but later, when there is a true surface diminution, the symptoms are, for reasons which will be seen later (page 163), considerably diminished.

A functional diminution of surface may be said to occur in pulmonary embolism and infarction. In these conditions the blood-vessels of a part of the lung become blocked and the surface supplied ceases to have a functional value. Later, as the result of the inflammatory condition and contraction of the scar, there may be true surface diminution.

In emphysema we have at first a greatly increased surface, but it has lost to a great extent its respiratory qualities, as the alveolar walls and the blood-vessels they contain suffer from tension and pressure effects. In more advanced cases there is actually destruction of the walls and a diminution of the respiratory surface results, although there may be an actual increase in the volume of the lung. There is then both oxygen want and carbon dioxide retention, which is further increased by the lack of adequate replacement of the alveolar air, the result of deficient expiration. Except in very severe and old standing cases, cavity formation in pulmonary tuberculosis is not sufficient to reduce the respiratory surface appreciably.

Replacement of Alveolar Air.—In order that the acquisition of oxygen and the elimination of carbon dioxide may be adequately carried out, it is necessary that the alveolar air should be maintained at a reasonably constant level. If this is not so, an adequate respiratory surface will be valueless. This constant level is at about 13 per cent. oxygen and 5–6 per cent. carbon dioxide.

At these percentages the hæmoglobin can take up almost its maximum amount of oxygen, and the blood can get rid of as much carbon dioxide as needed. The level of the latter in different individuals is remarkably constant, and is kept so by the activities of the respiratory centre. To enable these centres to do so the mechanism by which the operation is brought about must be acting properly. When we come to consider the anatomy of the lungs and respiratory passages it will be seen that the replacement of air and the bringing into action of the additional surface when required are dependent on the same factors. These are the mechanics of respiration, and the patency of the respiratory passages, while the vital capacity indicates their efficiency.

Mechanics of Respiration.—Details concerning this may be obtained from any physiological textbook. The main point to note is that the chest cavity is enlarged by muscular action. The ribs are raised, the sternum pulled forward, and the diaphragm descends or, what would be more accurate, in view of the fact that the central tendon does not move much, becomes more conical and less dome-shaped.

Obviously, then, any interference with the movement of the chest will interfere with replacement. This is fortunately a rare occurrence, but does sometimes occur in crowds. It is stated that in Moscow, in 1896, fifteen hundred people so perished in the crowds which assembled at the feasts in connection with the coronation. In the same category is death of infants by over-laying, even the weight of an arm of the parent being sufficient. In this instance exhaustion of the respiratory centre will also play a part. In emphysema, too, as stated above, a similar factor plays a part, as expiration is prevented by the increase in the volume of the lung. Should there also be any interference with the nerve supply of the muscles concerned, a similar condition of affairs will obviously be produced. This may occur in injury to the nerves, but is also seen in diphtheria, in which the toxin may affect the phrenic nerves only or the intercostals, or both. Artificial respiration and active treatment of the primary condition by anti-toxins is the only hope.

Death from strychnine poisoning or tetanus is of a similar nature. At each inspiration there is normally a reciprocal inhibition (see page 41) of the expiratory muscles, and at each expiration an inhibition of the inspiratory muscles. Large doses of strychnine, however, reverse the normal inhibition so that both sets of muscles pull at the same time. This renders the ribs almost immobile, and replacement of the alveolar air ceases. Death occurs in acute asphyxia in a few minutes after the onset of the convulsions due to a similar antagonism of the opposing muscles throughout the body.

Affections of the respiratory centre may be considered as making themselves effective through the nervous mechanism governing the mechanics of respiration. In the rapid shallow breathing associated with exhaustion of the respiratory centre, an exaggeration of the Hering-Breuer reflex, the faulty replacement of the alveolar air is really the method by which the aeration of the blood is brought about. This anoxæmia has been emphasized by Haldane, Meakins, and Priestley.

Interference with the movements of the diaphragm as the result of abdominal pressure is fairly common, as in ascites and cirrhosis. If the patient is already making every effort to make the best use of his respiratory apparatus, even normal abdominal pressure may embarrass respiration. All such individuals then benefit and are more comfortable by being propped up in bed instead of lying down, more especially cardiac cases, where the sitting position tends to relieve the right side of the heart, while the keeping up of the legs facilitates the return of blood from parts liable to œdema.

The Patency of the Respiratory Passages.—This is obviously essential for the adequate replacement of air, and we see the failure of this factor in laryngeal and tracheal obstruction. In these cases, not only is the air inadequately changed, but there is, as noted above, a tendency to fatigue the respiratory centre. Such occurs typically where foreign bodies have entered the respiratory passages, in œdema of the glottis, and in diphtheria. Here the symptoms rapidly become acute if untreated and the asphyxia results in death. Less acute cases fail from central fatigue. More chronic forms are seen in neoplasms pressing or obstructing the air passages or in bilateral abductor paralysis. In the chronic cases there appears to be a considerable amount of adaptation, which is dealt with on page 176. This is, however, extremely important should the surgeon decide to do a tracheotomy to relieve the breathlessness. A large number of patients so operated on die shortly after operation. It is to be presumed that such death is the result of lack of oxygen dependent on the inadequate stimulation of the respiratory centre. By relieving the obstruction the carbon dioxide in the alveolar air will be reduced and also that in the blood correspondingly. If the other adaptations are to act also, then too much carbon dioxide may be removed from the blood, so that the respiratory centre is inadequately stimulated. This will be further increased by a lessened sensitivity of the centre to carbon dioxide, which appears to be not improbable. An anoxæmia, then, analogous to that which occurs at low barometric pressures, will result.

In asthma, the obstruction is in the bronchial tubes, and all degrees of severity may be seen up to that of severe asphyxia, although it is very seldom

fatal. The individual is in severe distress, due to retention of carbon dioxide, but the symptoms depend on the extent to which the different tubes are affected. In those cases where the asphyxia is marked there is a noticeable carbon dioxide retention, and oxygen want, while the urine is acid.

An inflammatory lesion of the trachea and bronchi seldom causes respiratory obstruction, though lower down, as in broncho-pneumonia, this is more likely. Here at first there is an adequate surface, but the air of a large number of alveoli is not replaced. Venous blood, therefore, passes to the arterial side, great distress and cyanosis being evident. Should the condition progress and the alveoli become filled with exudation, the symptoms may be greatly reduced, provided the total surface reduction is not excessive.

Vital Capacity.—Of considerable importance in relation to the replacement of alveolar air is the vital capacity, i.e. the amount of air which after deep inspiration is expelled on forced expiration, normally about 2,500 c.c. The greater the vital capacity the less frequently will the air in the lungs require to be replaced, since the more air available the longer will it last of good respiratory quality, while, on taking a breath, the more will be replaced. Further, with a large vital capacity, there usually, but not necessarily, goes a large respiratory surface and both together increase the possible intake of oxygen and removal of carbon dioxide. There is described in physiological literature the instance of a well-known centre-forward whose normal rate of breathing was 4 to the minute and whose rate after maximum effort was 9 per minute. This individual in the process of training had greatly increased his respiratory surface, his vital capacity and power of replacement, and as his heart was also fully trained, it was impossible to make him out of breath.

The vital capacity may also be influenced (and can be readily shown experimentally) by the amount of engorgement in the pulmonary circulation. Several investigators have shown that in cardiac disease the reduction of the vital capacity is an indication of the cardiac efficiency. Some writers, e.g. Means, hold that such reduction plays an important part in the causation of cardiac dyspnœa. In view of the fact that in pleurisy with effusion there may be a great reduction of vital capacity without much dyspnœa breathing, such may be the result of other factors, such as irritation of the vagus. Clearly, dyspnœa from any cause will obviously be made worse by reduction of the vital capacity.

PULMONARY CIRCULATION

Although the lungs are equal in every respect to all respiratory requirements, unless the blood is pumped through them sufficiently often, there will

be a deficiency in the total amount of oxygen taken from the lung and delivered to the tissues in a given time. This has been called by Barcroft the stagnant form of anoxæmia. Owing to the deficient removal of carbon dioxide, the latter will accumulate throughout the body including the respiratory centre. This is a very common cause of breathlessness in cardiac disease. The failure is really one of the general circulation and all degrees are found; indeed it may be considered to occur temporarily in severe exercise in normal persons (pages 139 *et seq.*). The breathlessness of stout untrained persons to whom a small amount of exercise is relatively severe is probably also of this nature, although no doubt they also produce excessive amounts of carbon dioxide (page 295).

There is evidence that in cardiac disease circulatory impairment may lead to oxygen unsaturation of the blood, but this may in part be due to complicating factors affecting aeration. Whether or not from circulatory impairment only the aerating mechanism in the lungs may become deficient is a difficult point to decide.

That which determines the speed of pulmonary circulation is the right ventricle, whose efficiency depends on the amount of work it has to do. This work is determined by the amount of blood and the resistance against which it has to be pumped. Normally, the right ventricle is able to deal with all the blood reaching it from the veins, and provided the pulmonary resistance is not increased, it can do so. It has been seen in relation to cardiac failure that if the work of the ventricle has already been increased, by its having to pump against excessive resistance, or if the myocardium is weak, a very little additional work may prove too much for the organ. Frequently the primary cause of failure is increased resistance. This may be of two kinds: (1) actual diminution of the calibre of the blood-vessels, (2) increased *vis a fronte*, i.e. resistance to the onward flow of the blood consequent on impairment on the left side of the heart.

It should be realized that the normal ventricle can deal with very much more than the normal amount of work without difficulty. The response of the heart to effort has been fully dealt with (page 137). For example, it is possible to tie one branch of the pulmonary artery without any failure of the ventricle or without even affecting arterial pressure. This has actually been done in man as an emergency measure in severe pulmonary hæmorrhage. In conditions such as pneumonia, then, the cardiac failure which may occur is only partly due to increased resistance, although this is a large factor. The heart is already weakened by toxæmia and we have already seen that the rapid shallow breathing which exists in that condition may lead to anoxæmia, which further weakens the heart. In this way, too, the effect of the increased pulmonary resistance

in emphysema is emphasized by the effect of the latter condition on the heart. Here the alveolar walls are no longer fully capable of transmitting gases. They are degenerated and the blood-vessels are reduced, while not infrequently the pressure of the alveoli is continued by the original cause of the condition—coughing, the use of wind instruments, etc. Those of the Edinburgh School are familiar with "the three milestones" of bronchitis, so picturesquely named by Wylie:

1. Failure of acute bronchitis to pass off, and the inception of chronic bronchitis.
2. The production of emphysema as the result of the constant coughing.
3. Cardiac failure due to the emphysema.

In the final stages of emphysema there is increased breathing from a variety of causes—deficient pulmonary epithelium, inadequate replacement of alveolar air, and deficient action of the right ventricle. All of these tend to increase the amount of carbon dioxide in the blood and stimulate the respiratory centre, which is rendered abnormally sensitive by oxygen deficiency. A certain amount of adaptation (page 176) does occur, but thought this may ameliorate the symptoms for a time, the condition is usually progressive. This condition, at first pulmonary, is, in its final stages, one of cardiac failure.

The myocardium may be the seat of primary disease, such as chronic myocarditis, or fatty degeneration, when the pulmonary and systemic circulation are affected simultaneously.

The heart's action may be interfered with from without as in conditions such as neoplasms or pleurisy with effusion which press on the heart. It also occurs in conditions after pericarditis in which the pericardium has become adherent to the heart, and limits its movements.

One of the commonest causes of interference with the pulmonary circulation is impairment of the mitral valve. It may occur as a stenosis or an incompetence, the result of local disease, or from dilatation of the left ventricle consequent on aortic disease. By simultaneous records of the pressures of aortic, left auricular, pulmonary and venous pressures it has been found possible to study such disease. Particularly striking is the fact that in mitral incompetence (a usual accompaniment of stenosis also) the slightest variation of arterial pressure is followed by enormous changes in left auricular pressure. This is easy to understand when we remember that the pressure in the left ventricle is 40 to 50 times that in the left auricle. In exercise there is a double strain on the heart, for not only is there an increased venous return to the right side.

but there is an enormously increased resistance in the pulmonary circuit, due to its great congestion. It is therefore easy to see why such patients should be so breathless. The congestion must greatly reduce the vital capacity and prevent adequate ventilation. In some instances, especially in stenosis, the dyspnœa is due to the stimulating effect of the high pulmonary pressure on the vagus nerve endings.

General circulatory failure also affects the cerebral circulation indirectly, in so far that the blood reaching the centre may be surcharged with carbon dioxide. This will occur if the circulation is slowed down and the blood in passing through the tissues loses an abnormal amount of oxygen, and takes up more carbon dioxide than can be got rid of by its passage through the lungs. This will be still further evident during exercise, when the production of carbon dioxide is increased and the circulation becomes more inadequate.

THE GENERAL AND CEREBRAL CIRCULATIONS

A great deal of what has been said of the pulmonary circulation may be considered to apply to the cerebral circulation, in that cardiac failure may affect both. It will be seen, however, that alteration in breathing may occur as the result of change in the cerebral circulation quite independently of the pulmonary, although the effect of the latter on the blood may intensify the action. The respiratory centre itself requires a very small amount of oxygen in a given time. Alterations in the amount of blood therefore passing through the centre have little or no effect on respiration. Thus an individual may have his cerebral circulation so reduced that he faints and yet there is no breathlessness, as the respiratory centre receives sufficient oxygen from the small amount of blood which passes through the brain. In the same way in carbon monoxide poisoning there is little or no breathlessness at rest. The fact that the respiratory centre requires little oxygen is suggested by the small blood supply through the vertebral arteries, compared with the enormous blood supply of those parts responsible for consciousness. The latter require a large amount of oxygen in a given time and slight alterations therefore in the amount of blood that passes through the brain are extremely liable to cause fainting.

Should, however, the circulation through the respiratory centre be slowed to any appreciable extent the local carbon dioxide accumulates, oxygen lack is at once felt and the respiratory centre is stimulated. Thus is explained the well-known fact that individuals suffering from profound anæmia are quite conscious and free from distress at rest as the result of circulatory adaptations. Should, however, there be any attempt at exercise the circulation cannot respond

further, the cerebral circulation is not sufficiently fast to meet its requirements and extreme dyspnœa results. This is further discussed below.

Probably the best way to consider the response of the respiratory centre to oxygen is to imagine that it requires to be bathed in lymph which contains a very high percentage of this gas. The respiratory centre uses, however, very little oxygen and so long as the percentage is kept up little need be supplied. To keep up this percentage the concentration of oxygen in the blood must always be higher than that of the local lymph. Suppose, for example, that the blood has taken up in the lungs oxygen to the extent of 18.5 c.c. per cent. and that the respiratory centre is bathed in lymph containing 10 per cent. Then oxygen will be given off by the blood to the centre. If, on the other hand, the blood has taken up 9 per cent. of oxygen in the lungs, then none will pass from the blood to the centre, however much blood be supplied, and the centre will be rendered sensitive by its want. Thus we see why it is that breathlessness is a common accompaniment of the faulty replacement of alveolar air and also why there is breathlessness at high altitudes. In the latter case, the alveolar air may contain 13 per cent. of oxygen at a barometric pressure of 530 mm., which is only the equivalent of 9 per cent. at 760 mm. (see Appendix), and the amount taken up by the blood is reduced.

On the other hand, suppose the amount of *functional* hæmoglobin is very small, as in anæmia and carbon monoxide poisoning (where this gas prevents the hæmoglobin from taking up much oxygen), and it takes up 18.4 c.c. per cent. oxygen, although the blood will not take up so much oxygen per unit volume, it will give up a small amount of gas if exposed to lymph containing 10 per cent. This small amount will be quite sufficient for the respiratory centre and so long as it is supplied there is no breathlessness, although the total amount of oxygen supplied in a given time may be so small that consciousness is impossible. Thus we see that it is the concentration of oxygen in the blood to which the respiratory centre responds rather than to the amount available in a given time, or in more scientific language, the oxygen pressure rather than its mass.

Should, however, the cerebral circulation be inadequate, there will be local oxygen want, and carbon dioxide accumulation. The respiratory centre continues to use up slowly a small amount of oxygen and produces carbon dioxide, by which it is stimulated. This is well seen in hæmorrhage, in which respiration may be so stimulated that there is a reduction of the alveolar carbon dioxide, and a consequent reduction in the carbon dioxide in the arterial blood. This is also common in cardiac disease.

Cerebral Injury.—The cerebral circulation plays an important part in the

production of respiratory symptoms in which there is increased intra-cranial pressure, such as injury as in cerebral hæmorrhage, middle meningeal hæmorrhage or neoplasm. In these cases the effect is really due to anæmia of the medulla, the blood-vessels of which are compressed against the foramen magnum as the result of the brain being displaced downwards; such symptoms can easily be imitated experimentally and the obvious treatment is by trephining or other decompression operation. It is, however, to be noted that as pressure is not distributed equally through the different subdivisions of the cranial cavity, the trephine opening should be preferably in the subdivision in which the seat of the lesion is and, of course, should it be possible to remove the compressing agent, all the better. This will indicate that a neoplasm, although a very minute one in the region of the medulla, may produce symptoms out of all proportion to its size.

There is also evidence that the breathlessness of uræmia may be of a similar nature and it has been found by the Hæmoglobin Committee of the Medical Research Council that in uræmia there is not necessarily acidosis. Pal and also Mayer Bisch have pointed out that in such cases the dyspnœa is much relieved by lumbar puncture and that the cerebral spinal fluid may be under a pressure of 200 mm. mercury. Steps taken to reduce the blood pressure by vaso-dilators, severe purgation or bleeding and lumbar puncture may be of great value in tiding over an emergency.

The Blood as a Respiratory Tissue.—We have seen that if the respiratory centre is inadequately supplied with oxygen its sensitivity to carbon dioxide is increased. Since the oxygen is carried by the hæmoglobin, then we should expect that any inadequacy in the amount of the latter will produce a deficiency in the oxygen-carrying power of the blood. This may be seen in anæmia, and after hæmorrhage, where there may be a great diminution. In estimating the degree of anæmia the colour of the skin merely indicates as does the estimation of hæmoglobin the amount of the latter in a given area. If the total volume of the blood is increased, as Lorrain Smith has shown, in chlorosis, then the total hæmoglobin will not be much below normal, if at all. In other anæmias a small increase in blood volume is also common. In chlorosis, therefore, and where the volume is definitely increased, the blood supply to the brain does not fail so long as the circulation is capable of supplying the oxygen need. The greatly increased heart rate may make palpitation a most distressing symptom.

This excessive breathing must be brought about by increased carbon dioxide affecting the respiratory centre. An anæmic blood is not only deficient as an

oxygen carrier but also as a carrier of carbon dioxide. Largely due to the work of L. J. Henderson we know that the corpuscles by making alkali available are distinctly responsible for the carriage of carbon dioxide. Most of this gas is carried to the lungs as sodium bicarbonate, the sodium being made available from the sodium chloride in the plasma by the passage of chlorine ions into the corpuscles. If there is a shortage of corpuscles there must also be a shortage of the immediately available alkali in the blood as a whole, although not necessarily in the alkali reserve of the plasma. At the same time the oxygen deficiency of the blood will lead to an excessive production of lactic acid (formed from glucose during the contraction of muscle in the absence of sufficient oxygen), which will still further compete for the alkali.

When, in exercise, carbon dioxide is produced, not only will there be a diminution in the alkali side of the carbonic acid/sodium bicarbonate ratio, but there will be an extra amount of carbon dioxide in solution compared with that which normally occurs in exercise. The increased circulation by increasing the number of journeys done as it were by each unit of blood between the lungs and tissues may succeed in preventing an excess of carbon dioxide in the venous blood. In exercise, however, the circulation is unable to compensate any further, although more carbon dioxide and lactic acid are being added to the blood. The carbon dioxide content thus becomes abnormally high, and respiration is stimulated in excess of what would occur if the circulation rate could increase, as it does normally. Such breathlessness can be considered due to a relative circulatory insufficiency, akin to that found in cardiac disease. (See page 154.)

The Neutrality of the Blood.—Those who are unfamiliar with the method by which carbon dioxide is carried by the blood, and the neutrality of the body tissues maintained are advised to refer to Appendices B and C (page 349). For the present purpose it is sufficient to recall that this gas is carried to a small extent in physical solution, but mostly combined with sodium as bicarbonate. That in solution is slightly acid, while that in the form of bicarbonate is faintly alkaline. The neutrality of the blood may be looked upon as depending on the ratio

$$\frac{\text{carbon dioxide in solution}}{\text{carbon dioxide as bicarbonate.}}$$

Should, however, there be any impairment of the mechanisms by which acids are normally got rid of, or if abnormal acids are produced, these may compete with the carbon dioxide for the available alkali. More carbon dioxide will be

thrown into solution, which will be excreted by stimulation of respiration. The respiratory mechanism plays an important part in the maintenance of body neutrality. Conversely, the factors on which the latter depends help to determine the rate of breathing.

In conditions in which the liver, kidney or pancreas is diseased there is often an upset of the mechanisms controlling body neutrality, and the characteristic breathlessness is the result.

The Quality of the Air Breathed.—This is included for the sake of completeness, but it is of comparatively little clinical importance, although it is of enormous interest to physiology and hygiene. The air may itself contain an excess of carbon dioxide, but it has now been definitely shown that this possibility has been exaggerated, that carbon dioxide in the most stuffy room rarely exceeds 1 per cent. and no serious effect on respiration is appreciable until it has reached 4 per cent. It is now clear that the factors which cause the so-called stuffiness in a room is stagnation of air and that if the air is kept in movement it is no longer disagreeable. (Leonard Hill.)

The air may contain less oxygen and carbon dioxide than normal, but this only occurs at high altitudes or in special chambers. In these circumstances the relative percentage of oxygen and carbon dioxide may remain the same, but at the lower barometric pressures 21 per cent. of oxygen will not represent the same amount of oxygen as it does at sea-level, where the molecules of the gas are more compact.

The air may contain poisonous substances which may irritate the respiratory passages (e.g. chlorine) and cause them to secrete to an excessive extent or, by causing bronchial spasm, interfere with the replacement of air.

The inspired substance may be absorbed and cause death by central action (e.g. prussic acid gas) or it may combine with the hæmoglobin and reduce the oxygen-carrying power of the blood as carbon monoxide or coal gas or exhaust gases. Not only does the carbon monoxide prevent oxygen from being taken up, but it also causes the hæmoglobin to hold on more firmly to its oxygen, producing a severe form of anoxæmia which commonly causes death. Even if death is not caused there are usually serious nerve symptoms. The memory and mental powers may be seriously upset, indeed every organ of the body may be left impaired and in particular the blood supply to the heart. Partial carbon monoxide poisoning has been mistaken for alcoholism.

The principle of treatment is to remove the individual from the poisonous atmosphere and at the same time to keep him warm, as cold tends to aggravate anoxæmia in the same way as it does shock. At one time the stability of carbon

monoxide hæmoglobin led to the belief that it was not dissociable at all. This, however, has been shown not to be the case, a fact which indicates that cases of carbon monoxide poisoning are not hopeless until they are dead. Artificial respiration may be necessary and the administration of oxygen is most desirable, as it facilitates the dissociation of the abnormal hæmoglobin compound.

When we have considered the factors on which breathing depends, we realize what was stated in the first few words of the chapter, namely, that breathing is the demand of the tissues for the supply of oxygen and the elimination of carbon dioxide. The tissues make the demand by the amount of carbon dioxide which is produced in activity. The carbon dioxide message is carried by the blood to the respiratory centre, which in turn activates the necessary mechanisms and answers by sending the required amount of oxygen to the tissues, while certain other interrelations exist. The effect of the higher centres on the respiration may be such that the arrival of the message is anticipated and the breathing, together with the circulation, is hastened in advance.

Respiratory Efficiency.—From what has been said above it is evident that the ultimate evidence in the efficiency of respiration lies in the investigation of the oxygen and carbon dioxide content of the blood, by taking actual samples from an artery. While this may be possible in hospital, it, of course, is quite out of the question in ordinary practice and, at the best of times, it has to be remembered that although venous puncture is practically painless, arterial puncture may be exquisitely painful. The general practitioner must rely on the ordinary clinical examination of his patient, but in making such an examination it will be evident from what has been said above that a very large number of factors have to be remembered when a breathless patient is being considered. It is true that fortunately the excellent correlation and post-mortem findings have resulted in an almost perfect system of diagnosis so far as the pathological condition present is concerned, and we owe much to the pathologists in this respect, a fact possibly too often forgotten. It is, however, essentially in the treatment that the benefits of our knowledge of the mechanisms of symptom production is best seen and, after all, the symptoms are the complaint of the patient for which he primarily seeks relief.

The best indication of the potential respiration efficiency of the normal individual is probably the vital capacity. This has already been dealt with on page 154. The general respiratory efficiency, i.e. the efficiency of all the mechanisms responsible ultimately for the maintenance of general tissue oxidations, is indicated by the effect of exercise. Impairment of any of these mechanisms usually gives rise to breathlessness out of proportion to the exercise taken.

CHAPTER XIX

CYANOSIS AND BREATHLESSNESS. ANOXÆMIA AND OXYGEN THERAPY

CYANOSIS AND ITS RELATION TO BREATHLESSNESS

From what has been written with regard to the factors of respiration it is evident that breathlessness or dyspnœa may result from a variety of causes. It may be made more evident by exercise as the additional carbon dioxide produced accentuates failure of the respiratory mechanism. Ordinarily a patient complains of shortness of breath, when he is inconvenienced by the rate and depth of his breathing. He may, however, have considerably increased respiration, but become so accustomed to it that he fails to notice it, and makes no complaint. We shall see further that he may show every evidence of failure in the respiratory mechanism, e.g. the cyanosis of congenital heart conditions and yet for reasons given below he may not be short of breath. On the other hand, there may be breathlessness without cyanosis, as in the anæmias. Breathlessness does not necessarily indicate oxygen want or the retention of carbon dioxide, although it usually does, while these conditions may exist without there being breathlessness, as, for example, when the respiratory centre is thrown out of action. Nor need oxygen want or the retention of carbon dioxide exist together when there is breathlessness. Either is sufficient to cause the breathlessness. It is clear, then, that breathlessness, although closely allied to and commonly associated with cyanosis, must be looked upon as quite distinct.

Cyanosis is due to an excessive amount of reduced hæmoglobin as distinct from oxyhæmoglobin circulating through the skin and mucous membranes. It may be due (1) to imperfectly aerated blood circulating in the arteries; (2) to a local stagnation or slowing of the circulation in the vessels concerned so that the blood passing through these regions loses an excessive amount of oxygen.

The circulation of imperfectly aerated blood will result from any condition in which the aerating mechanism of the lung is inefficient or is short-circuited. In both conditions there is invariably breathlessness except in long-standing cases where a marked degree of adaptation has occurred. The cyanosis becomes apparent in any condition which interferes with the replacement of the

alveolar air. This, as we have seen, may be due to a reduction in the patency of the respiratory passages, such as may occur in severe bronchitis, laryngeal abductor paralysis or in asthma, since the venous blood in passing through the lung or certain areas of the lung fails to become oxygenated.

It is, however, very striking what curtailment of respiratory efficiency can occur without there being either cyanosis or appreciable breathlessness, as when the lung becomes consolidated, especially as a result of pressure from without. Thus in the more chronic type of pleurisy with effusion, in which the fluid is slowly thrown out, collapse of almost a complete lung may take place with so little respiratory distress that the physician is often surprised when he discovers the extent of the effusion. The absence of signs and symptoms in the latter is due to the fact that in the areas affected not only have the airways been closed but the pulmonary circulation has also been cut off. The blood which does pass through the lung, therefore, passes through the walls of fully aerated alveoli and therefore is fully oxygenated until at least more than one lung is thrown out of action and the replacement of alveolar air becomes inadequate. It is now generally agreed that pleurisy with effusion is often if not invariably of tuberculous origin and a very curious position has arisen. On the one hand it has become common practice to produce an artificial pneumothorax and so to rest an afflicted lung, while on the other there are few who are prepared to look upon an effusion as having a similar protective function.

In pneumonia the following sequence of events is often seen. In the first day or two the patient is extremely breathless and often cyanosed, since venous blood passes through to the arterial side unchanged as a result of faulty replacement of alveolar air. This is caused by shallow breathing consequent on exaggeration of the Hering-Breuer reflex and by a blockage of the bronchioles in the area affected. When, however, the consolidation becomes more complete, the patient obviously becomes easier and of a better colour and continues to be so if all goes well. Sometimes, unfortunately, a severer form of cyanosis may ensue, the patient becoming an ashen grey colour, which is of grave significance, and may be due to several causes. The lesion may have so progressed that now the lung surface and replacement of alveolar air are insufficient for adequate aeration, as is seen particularly in influenzal pneumonia where post-mortem the bronchi are found to be blocked with fluid. The Oxford School have emphasized the importance of continued shallow breathing in such cases and the anoxæmia produced thereby. This breathing is held to be the result of the existing anoxæmia which in itself accentuates the shallow breathing.

The irritation of the vagus endings in the lung (see page 157) and the increased sensitivity of the respiratory centre probably contribute. However produced, there can be little doubt, as indicated by Haldane, that such breathing must lead to faulty aeration of the lung alveoli with attendant reduction in the aeration of the blood.

Another common cause of this late cyanosis is right ventricular failure due to the toxæmia and probably anoxæmia of the cardiac muscle with increased pulmonary resistance, and there become superimposed upon the original condition, the signs and symptoms of cardiac inefficiency. So important do some physicians consider this factor in pneumonia that at the very beginning they do all they can to relieve or improve the right side of the heart.

The right ventricular failure of any appreciable degree marks the failure not only of the pulmonary circulation but of the circulation in general. A general slowing of the circulation is the result and especially is this so in the capillaries where by giving more time for reduction of the hæmoglobin it tends further to produce cyanosis. The cyanosis which accompanies chronic venous congestion of cardiac disease and which accompanies œdema is of this nature. One of the most severe forms of cyanosis is that of congenital heart disease where part of the blood is short-circuited through a patent foramen ovale. The cyanosis will depend on the actual degree to which the blood is short-circuited and all varieties are seen, although the severer cases seldom attain adult life. It is often striking what a severe cyanosis may exist with little or no breathlessness. This is because the blood which does pass through the lungs is more capable of carrying oxygen per c.c. because of the increased number of red blood corpuscles, but although there is an increased amount of reduced hæmoglobin in the mixed arterial blood, there is not necessarily an appreciable increase in carbon dioxide, as this may be got rid of otherwise, e.g. as carbonate in the urine. There are also certain other adaptive mechanisms which exist in other parts of the body.

Cyanosis and dyspnœa in a somewhat peculiar form are also characteristics of asthma.

This condition appears to be the result of an upset of the normal mechanism of respiration.

Coke and Negus, who have studied the subject independently, agree that the function of the bronchioles is to contract during expiration, with a view to diminishing this dead space, and so facilitating the respiratory exchange. Coke considers that the bronchiolar contraction prevents a complete emptying of the alveoli. The older idea of the protective function of the bronchioles does not,

especially in view of the investigations of Negus (on the comparative anatomy of the respiratory passages), seem tenable. Animals which could not normally be exposed to dust, etc., have excellent bronchial and tracheal muscles. Especially is this so in running animals. The suggestion that the bronchi contract during expiration is further supported by the marked diminution in the lumen of the bronchi. This may readily be seen through the bronchoscope. It is also extremely difficult to remove a foreign body from a bronchus during the expiratory phase. In anaphylactic shock guinea-pigs die from acute overdistension of the lungs (Muir). This observation does not appear to have been correlated with emphysema and the fact that in asthma there is difficulty in expiration rather than in inspiration. It is generally agreed that many cases of asthma are probably anaphylactic in nature. It is known that asthmatics are specially liable to become anaphylactic to therapeutic sera, such as antidiphtheritic serum.

Experimentally it is very difficult clearly to distinguish between active constriction of bronchioles and passive movements as a result of those of the chest wall. By analogy with the larynx, which can be shown to close at the onset of expiration (Negus and McDowall), it seems justifiable pending absolute proof to support the conception that the bronchioles actively contract during expiration, and that the closure is either excessive or badly timed in asthma. The difficulty in expiration seems to make the patient afraid to take a breath. As a result of the faulty replacement of the alveolar air, cyanosis may result.

The well-known effect of adrenaline in relieving the condition indicates that there is an increased parasympathetic activity which can be counteracted by sympathetic stimulation. It is doubtful whether other forms of sympathetic stimulation such as exercise during the attack, the administration of carbon dioxide by reinhalation of the expired air or the production of more acid by dietetic and therapeutic means have been sufficiently tried. There is no doubt that the production of a physiological dyspnœa can cut short an attack. Similarly, the physiological sympathetic stimulation which occurs in pregnancy (see "The Balance of the Endocrine Organs," Chapter XXXIX) often results in a complete freedom from the attacks. They may return, however, very soon after the puerperium.

Treatment of the underlying condition is often an extremely difficult matter, for the asthmatic state appears to depend on a great variety of causes. Some cases have been shown to be instances of sensitization to foreign proteins, or association with feathers, fur, horse dandruff, and the like.

Some are just as clearly influenced by atmospheric conditions and others are

the result of irritation of the respiratory tract as in chronic bronchitis. Finally it must be emphasized from the physiological point of view that the nervous mechanism of bronchiole control is apparently upset. It is generally agreed that there is often a psychological element in such cases—two facts which may not be without a significance.

ANOXÆMIA

In the preceding pages oxygen lack or anoxæmia has been frequently mentioned. It is of the greatest importance in medicine, although it may be looked upon as a pathological condition discovered by the physiologists. We owe our beginnings of knowledge of the subject to the school of J. S. Haldane whose words on the condition indicate its seriousness:

"Anoxæmia not only stops the machine but it wrecks the machinery."

At the post-mortem, the effect of local anoxæmia has long been known, but it is only of recent years that the effects of general anoxæmia have been clearly recognized. All tissues suffer as the result of oxygen want, but some tissues more than others, and experience shows that nervous tissues are particularly sensitive.

The types of anoxæmia which are met with may be divided into three groups, and Barcroft in describing them has adopted a homely simile. He compares oxygen supply to milk supply and points out that there are three causes which may conspire to deprive your family of milk:

(1) There may not be enough milk at the dairy. (2) The milk is adulterated and what is sold is not really milk. (3) The milkman from that particular dairy may not call.

These three classes he calls the anoxic, the anæmic, and the stagnant types of anoxæmia.

In the anoxic type the blood is normal but does not take up sufficient oxygen in the lungs. There is a deficiency in respiratory surface, in replacement of alveolar air, or the quality of the air is insufficient. This latter will include failure of the respiratory centre. In the anæmic type we have failure of the blood to carry sufficient oxygen, while in the stagnant variety there is faulty transport of normal blood which may contain the normal amount of oxygen.

In anoxæmia we look upon oxygen want from the point of view of the tissues rather than from the breathing. It must be clear that anoxæmia is quite distinct from carbon dioxide retention, with which it may or may not be coincident. Anoxæmia may exist with normal or diminished carbon dioxide in the blood.

An anoxæmia without carbon dioxide retention may readily be produced by forced breathing. This procedure washes out the excess of carbon dioxide from the lungs and that of the blood is similarly reduced, with the result that the respiratory centre loses its normal stimulus and there is a period of apnœa (a period during which there is no desire for breath). The oxygen in the blood becomes used up during the apnœic period and before the carbon dioxide has accumulated in the tissues sufficiently to stimulate the respiratory centre the tissues may be seriously affected by the oxygen want.

A similar anoxæmia without carbon dioxide retention is seen in carbon monoxide poisoning, where the hæmoglobin prefers this gas to oxygen and there is rapid oxygen want. This increases the sensitivity of the respiratory centre and the normal carbon dioxide stimulates the respiratory centre to increased activity, so that the amount of the latter in the blood becomes much reduced. The anoxæmia which is the limiting factor in life at high altitudes is similarly associated with excessive loss of carbon dioxide which results from the low barometric pressure and the earlier hyperpnœa of the oxygen want. The fall of carbon dioxide in the blood which occurs in lobar pneumonia where the severe dyspnœa of the first few days has passed off, is of a similar nature and due to the hyperpnœa caused by the slight anoxæmia which may still persist.

In all those conditions the anoxæmia of the tissues is further accentuated by what is known as the Bohr effect. Not only does the reduction of carbon dioxide prevent adequate stimulation of the respiratory centre, but just as we have seen that carbon dioxide assists dissociation, so also does lack of carbon dioxide prevent the hæmoglobin from giving up oxygen. It must, however, be admitted that oxygen want, with at the same time a reduction of carbon dioxide, must be considered a circumstance for which the body is not prepared, as the Bohr effect suggests. Such states cannot be considered in any sense physiological. They might be considered the result of civilization. It is true that in excessive breathing in emotion there is certainly carbon dioxide loss, but this may be looked upon as a preparation for activity and excessive production of carbon dioxide. Where there is carbon dioxide loss the body attempts to restrain otherwise its output of acid. Thus we find the urine becomes alkaline as the kidney reduces its excretion of acid sodium phosphate and excretes more of the alkaline salts. In the same way no ammonia is required to assist in the excretion of acids and the ammonium salts in the urine are reduced with a corresponding increase in urea.

The physiological principles in such cases are obviously the administration of oxygen and carbon dioxide, the latter being most easily brought about by

the individual rebreathing a certain amount of expired air to which oxygen has been added. This is exactly the procedure adopted in climbing high mountains.

The type of anoxæmia for which the body is particularly well prepared is that which is accompanied by carbon dioxide retention. This is well seen in severe exercise and thereby the body is capable of considerable muscular activity in emergency when perhaps breathing is impossible. Muscular contraction can take place in the absence of oxygen, which is only required in the recovery process. Such contraction must, however, be considered uneconomical, as the lactic acid formed is incompletely utilized and passes into the blood. It is possible then for the muscles to do more work than oxygen can be supplied for during the actual period of activity. There is indeed an oxygen debt which can be paid up as it were at a more convenient period. Thus we see a sprinter may run a hundred yards without taking a single breath. During that period, however, the accumulation of lactic acid raises the hydrogen ion concentration of the blood and causes greatly increased respiration as soon as the sprint is over. The oxygen debt may be looked upon as a physiological anoxæmia, as it is evident that the body is well adapted to deal with it. The lactic acid is rapidly excreted as lactates in the urine and at the same time the various organs responsible for maintaining body neutrality increase their activity, the kidneys excrete more acid phosphate and more acid as ammonium salts with a corresponding less amount of urea, the lungs get rid of more carbon dioxide and the intestines retain more alkaline phosphate.

This is a common type of anoxæmia met with clinically. In this category are those cases of oxygen want which occur from inefficient ventilation, such as failure of the mechanism for replacement of alveolar air and diminution of respiratory surface. The hæmoglobin is unable to take up its full charge of oxygen, insufficiently aerated blood circulates in the arteries and the individual is very cyanosed and breathless. So far as the hæmoglobin is concerned, the condition is similar to that seen in life at high altitudes, and, according to Barcroft's classification, is considered of the anoxic type. We may then have two kinds of anoxæmia due to a similar cause so far as the hæmoglobin is concerned, i.e. insufficient saturation in the lung, but in one there is carbon dioxide retention which helps to counteract the oxygen want and in the other (altitude) the condition is aggravated by the coexisting loss of carbon dioxide. In both there is cyanosis from a diminished amount of oxyhæmoglobin compared with the amount of hæmoglobin.

In the anæmic type of anoxæmia there is insufficient functional hæmoglobin in circulation. There may or may not be breathlessness, but there is no cyanosis,

as all the blood which passes through the lungs is fully aerated. In carbon monoxide poisoning we have seen there may be diminished carbon dioxide in the blood from the initial hyperpnœa, for as a result of the increased sensitivity of the respiratory centre due to oxygen want the breathing settles down to a new carbon dioxide level which is below normal. In the anæmias, however, as stated in the previous section (page 160), there is considerable adaptation on the part of the circulation and it is not until this becomes inadequate that there is actual anoxæmia. Thus anæmic people may be quite comfortable at rest but quite incapable of even moderate exercise.

That individuals who suffer from severe anæmia retain consciousness is scarcely what at first sight would be expected. It is explained by the fact that as a result of the adaptation of the circulation the total amount of oxygen supplied to the cerebrum is sufficient. In carbon monoxide poisoning, on the other hand, the total oxygen available in a given time is reduced, and, further, the carbon monoxide prevents the hæmoglobin from giving up its oxygen to the tissues, including the heart, which latter therefore fails and causes a fall of blood pressure. This adds to the lack of oxygen, and the individual may become unconscious.

The stagnant type of anoxæmia is seen typically in cardiac failure where there is marked slowing of the circulation. A similar condition of affairs will occur when the blood volume is reduced, as it may be by hæmorrhage, when the reduction is actual, or in secondary wound shock where the reduction is relative. If it is due to cardiac failure, the anoxæmia is accompanied by cyanosis, the result of the backward pressure, and breathlessness as the result of the slowing of the circulation. This type of anoxæmia may result from local stagnation consequent on obstruction through the arterial supply of the part, or to the venous return. When there is loss of blood volume every effort is made by the body to maintain the cerebral and pulmonary circulation even at the expense of the less important parts. It is found that if an animal is bled, the blood pressure does not immediately fall, but it may be shown that the limbs are constricted to make up for the loss of blood. At the same time, also, loss of blood prevents activity, little heat is produced and the skin vessels are little required. Clinically, the pallor of the skin in such cases is very evident.

The Symptoms of General Anoxæmia.—These are as yet so little recognized that it requires little excuse to include them in this volume. Anoxæmia inhibits full activity of all tissue, and many symptoms hitherto badly understood are merely those of disguised oxygen want. For example, indigestion,

so called, is often the result of a poor gastric circulation. The symptoms discussed here are those which have been demonstrated by physiologists as the results of breathing rarefied atmospheres in evacuated chambers, in climbing mountains, in rebreathing from confined vessels and in breathing carbon monoxide or observing the results of cases of poisoning.

The effect of sudden anoxæmia may be most dramatic and fatal. This is most frequently seen when attempts have been made to enter disused wells, mines, pits and such-like in which there has been an accumulation of carbon dioxide. Instances have occurred in which a man has suddenly become unconscious and fallen when descending a ladder into such a place, and a similar fate has overtaken several rescuers. In such cases the carbon dioxide may be almost undiluted, and apparently the individual did not suffer from warning symptoms. More usually the anoxæmia seen in disease is slow in onset. Pulse and respirations are stimulated for reasons explained in the preceding pages, and if, at the same time, there is carbon dioxide retention, as there is most frequently in clinical cases, there is also a marked cyanosis. When, however, there is loss of carbon dioxide, the cyanosis is obviously no guide to the degree of anoxæmia present, and this in the past has frequently been misleading, although fortunately such conditions are not commonly met with.

The nervous system is specially apt to be affected even without the knowledge of the patient, although the severity may not be sufficient to cause actual loss of consciousness. Records of balloon ascents indicate that the senses, memory and judgment may be seriously impaired even to the extent of endangering life. The intrepid balloonists Crocé-Spinelli, Sivel and Tissandier in 1875 continued to ascend until two of them actually died, although means for their immediate descent were at hand. Experience after mine accidents also indicates that those who, at first sight appear normal, may do quite irrational acts and may simulate the condition of an alcoholic. Clinically, restlessness, such as seen after hæmorrhage, is common and all stages from being "slightly off" mentally to delirium and coma are seen. In severe anoxæmia the effect of oxygen want is particularly felt by the respiratory centre which rapidly becomes exhausted. Periodic breathing of the Cheyne-Stokes type often heralds the end which is brought about by the central failure.

In the more chronic forms of anoxæmia the mentality shows evidence of fatigue, and the individual may become very irritable and almost a neurasthenic. Clinically, the local effects of such anæmia are fairly common.

Local Anoxæmia.—Here again the onset may be sudden as when there is blockage of an artery from an embolus. Briefly, the symptoms of such a

blockage must depend on the organs actually affected and on whether or not a collateral circulation can be established. The acute pain which may be felt is considered to be due to spasm of the artery wall which we now know from experimental puncture of arteries is extremely painful. The rate at which collateral circulation is established is often very great and it may be reasonably efficient. Thus, for example, in embolus of the axillary artery, the circumflex artery may become the main artery of supply to the arm. In areas where such collateral circulation does not exist, such as the cerebrum, the damage is in the nature of things permanent unless as a result of organization of the embolus the lumen becomes again patent. Similar effects may result from temporary pressure on an artery and it is extraordinary how symptoms will persist, such as muscle weakness or still more nerve weakness from pressure in the brain, even when the anoxæmia has been of comparatively short duration. Spasm of blood-vessels may in the same way bring about local anoxæmia which may or may not cause serious damage to the tissues. Spasm of the retinal vessels as is sometimes seen after quinine may give permanent blindness, while in Raynaud's disease the tissues of the fingers may eventually become gangrenous. Some consider that the slowly deleterious effects of epileptic attacks on the brain are of similar nature and the symptoms of an epileptic seizure can readily be explained as indicative of arteriospasm, although many factors may be concerned in producing such spasm.

Local anoxæmia may, however, be brought about as a protecting mechanism to conserve heat. The blue hands and blue ears so noticeable on a cold day are brought about in this way. Here the arterial constriction prevents the blood reaching the skin and being cooled, while the blood in the capillaries loses its oxygen and becomes markedly venous in colour. In this respect it must be remembered that the ordinary pink colour of the white races is due to the presence of arterial blood in the skin capillaries.

Should the anoxæmia be the result of venous obstruction, the effect on the capillaries is very striking. The permeability of the vessel wall is markedly increased and fluid passes from the blood into the tissues, giving the clinical condition of œdema. It has been shown quite clearly by Bolton and others that if the venous return to a part is obstructed, the œdema is not produced necessarily during the time of the obstruction but may increase appreciably for a time after the obstruction has been removed. Also as a therapeutic measure in ulcers of the leg it has been claimed that local applications of oxygen such as placing the limb in an atmosphere of the gas brings about improvement. Where the circulation is normally slow, as in the feet, we find œdema particu-

larly liable to occur, and where there has been obstruction to the veins, the œdema is accompanied by distension of the peripheral veins. The fact that œdema is not a marked feature of arterial obstruction is explained by the diminished capillary pressure which occurs at the same time. Should, however, the obstruction be temporary it may be expected that the stage of pallor will be succeeded by a stage of swelling, as in Raynaud's disease.

OXYGEN THERAPY

Few methods of treatment so obviously necessary have given such unsatisfactory results in the hands of the unskilled. Failure has largely been due to faulty methods in the administration of oxygen or to attempt to secure improvement where none could be expected, often indeed when it is too late. It would be well, then, to consider the conditions under which oxygen therapy may or may not be of value. We have seen that if the blood is exposed to a mixture as it is in the alveoli containing 13 per cent. of oxygen, it is practically saturated, that is, it takes up the maximum amount of oxygen it is capable of acquiring. Even if the blood is only 90 per cent. saturated, which would occur with 9 per cent. oxygen in the alveoli, the individual is fairly comfortable, but it has been shown that below this figure the individual may show signs of breathlessness and mental symptoms indicative of oxygen want (anoxæmia). If then the patient suffers from a condition which seriously interferes with the replacement of alveolar air which will reduce appreciably the oxygen in the alveoli, the administration of oxygen will obviously be of value. This has been discussed on page 151, where it is seen that obstruction in the respiratory passages as in bronchitis, and the rapid shallow breathing of pneumonia and mitral disease, are particularly effective in preventing ventilation of the alveoli. There is no doubt that in such cases oxygen therapy is of great value and that the oxygen circulating in the blood is appreciably increased has been shown by actual investigation, largely by Meakins.

If, however, the general alveolar air is approximately normal, no advantage can be gained by increasing the oxygen percentage in the air breathed so far as the hæmoglobin is concerned, as it is already saturated, at least that which is actually exposed to the air. But, as we have seen, a certain amount of hæmoglobin may not be exposed if certain of the alveoli or bronchioles are blocked and the venous blood gets through to the arteries. The saturation of the mixed blood will then be low. Oxygen therapy in such cases must depend on the amount of oxygen which the increased percentage causes to be taken up, not by the hæmoglobin, but by the plasma. The greater the percentage in the alveoli,

the more will be taken up by the plasma, according to the Henry-Dalton Law.

The essential principle of oxygen therapy is therefore that the oxygen percentage in the alveoli must be increased to a maximum and all methods of administration which do not effect an approximation to this are useless. It used to be thought from experiments on small animals that breathing of high percentage of oxygen would cause pneumonia, but now there is ample evidence even on a prolonged administration of oxygen that this is not so. One point in relation to pneumonia may also be of importance, that is the pneumococcus is particularly sensitive to oxygen which inhibits its growth. Some have considered that the hæmoglobin may be able to take up oxygen from pathological accumulations of fluid in the alveoli if that fluid is saturated with oxygen. When one considers the slight solubility of oxygen in such fluids it is difficult to see how this can be brought about. Direct solution in the plasma in unaffected alveoli is another matter. After all, the hæmoglobin gives off its oxygen to the tissues by way of the plasma and the more that fluid holds in solution itself the more will it give to the tissues.

Methods of administering oxygen are various and for general purposes perhaps the original method is the best, namely, the taking of oxygen into the air passages by means of a tube. Let it be said at once that the so-called funnel method is of no value, as it does not really enrich the inspired air appreciably, most of the oxygen, being heavier than air, being spilt from the funnel. The administration of oxygen through a nasal catheter, one nostril being blocked, is a method very generally applicable and is efficient, but unfortunately wasteful. The waste, however, can be materially reduced if an attendant is made to pinch the tube on each expiration. The more an attempt is made to economize automatically the oxygen, the more apparatus is required, and it must be remembered that pneumonia patients—and that is the usual class requiring oxygen—have a sensation of want of air and anything which adds to this is not well tolerated. The apparatus of Haldane which has a close-fitting face mask has this as its aim. There is no doubt that it is efficient, but authoritative opinion is divided regarding its comfort. For hospital use it is possible, but it is doubtful to what extent the patient's friends could be persuaded to allow this procedure in private practice. However, if oxygen is given it must be given freely; according to Meakins, who has used both methods, the oxygen should be given through a tube 1 cm. in diameter and bubbled through a fluid at such a rate that the bubbles cannot be counted.

The use of special oxygen chambers on bed tents is ideal theoretically, but

here again we have difficulty in attending to the wants of the patient whose dry mouth and lips constantly require attention and add considerably to his discomfort. Unless then the chamber is sufficiently large for attendants to get inside the value of such chambers is limited. Bed tents are also notoriously apt to leak and waste oxygen.

Much of the discredit of oxygen therapy, as stated above, is the result of faulty administration, but in efficient hands there is now ample evidence of its great value.

It is further essential not to delay until anoxæmia is extreme. Lack of oxygen favours the growth of most organisms, especially the pneumococcus, while it weakens the heart and the excessive breathing tends to exhaust the respiratory centre. Reference has already been made to the vicious circle which must be broken. So it is seen that if oxygen treatment is not a routine it should always be given early where the prognosis is bad and before there is cyanosis, while it must be continued until there is definite evidence that anoxæmia has disappeared.

More recently Yandell Henderson has pointed out the value of the recumbent position in reducing the arterio-venous oxygen difference since it increases the circulatory rate out of proportion to the demand for oxygen. The necessity of reducing muscular activity to a minimum is evident.

CHAPTER XX

THE GENERAL RESPIRATORY ADAPTATIONS OF THE BODY. THE RESPIRATORY PROTECTIVE REFLEXES

THE GENERAL RESPIRATORY ADAPTATIONS

Although, unfortunately, it is only too common to consider respiration, circulation and the blood as separate systems, it is especially important in clinical medicine to realize that they really form together the *general respiratory mechanism.* It is true that the circulation, for example, may be considered as part of the general nutrient system, but clinically this is of little importance compared with its function in relation to respiration, since it is impossible for the body to store sufficient oxygen to keep it alive for ten minutes.

It is seen that certain adaptations may exist in each part of the general mechanism responsible for the supply of oxygen and the elimination of carbon dioxide that they may become more efficient should there be any such demand. These adaptations are normally those which can be utilized in exercise, but they are specially important as they provide a margin of reserve which may be and is used in disease, when it is seen that they are apparently directed at the distribution of the load whether it be oxygen want or carbon dioxide retention. These adaptations are now considered in relation to the organs where they are found.

The Lungs.—Whenever any part other than the respiratory system proper breaks down, respiration tends to be increased, as has been already noted. It must be obvious, however, that increased breathing has many disadvantages and in particular that it limits the respiratory reserve available for increased activity. Later on an enormous increase of breathing must itself be exhausting, and, in view of the muscular activity required, must tend to increase to a large extent the production of carbon dioxide. Increased breathing, then, is a temporary or first-line defence against breakdown, but every effort is made by the body to reduce the breathing required, and to maintain a pulmonary reserve if the failure is a prolonged one. To make this possible we shall see that adaptations on the part of the circulation, blood and the excretory system take place.

Local adaptation of the lung itself may occur. We have already seen that should any part of the surface or replacement of alveolar air be interfered with,

the increased breathing itself brings increased surface into operation. This is seen as a compensatory emphysema which is found where a part of the lung is compressed by a pleuritic effusion or in pneumonia. The occurrence of such an emphysema often, indeed, leads to the diagnosis of a deep-seated or otherwise unrecognizable consolidation. According to some authorities, too, it is held that the pulmonary epithelium is, in cases of emergency, capable of actually secreting oxygen into the blood, but this is not as yet generally accepted. Use is made of the general respiratory mechanism when the other factors of respiration fail, such as the mechanism for the transport of oxygen and carbon dioxide, or for the regulation of body neutrality. The way by which the increased respiration is brought about is dealt with in relation to breathing, and we shall see that similarly the other factors respond when respiration fails.

Circulation.—In the circulation we have further lines of defence, which may be brought into operation if other parts of the general respiratory mechanisms become inefficient. Should, for example, the oxygen-carrying power of the blood be reduced, the lungs fail as respiratory organs, or the liver and kidney cease to play their part in acid excretion, the heart is markedly hastened and the circulation rate increased. The blood passes through the lungs more frequently, so that the normal amount of oxygen may be carried to the tissues in a given time and the normal amount of carbon dioxide eliminated. As we have seen in relation to the rate of the heart, this hastening is brought about quite automatically by the carbon dioxide which tends to accumulate and it is interesting to note that the increased circulation rate is brought about exactly as in exercise. The carbon dioxide by stimulating respiration facilitates the return of blood to the heart, it acts in the veins directly and through the vasomotor centre, these factors combining to raise the venous pressure which brings about the increased rate of the heart. This was shown by Bainbridge to be a result of the reduction of vagus tone, and a stimulation of the sympathetic system due to increased pressure in the right auricle.

This increased heart action hastens the circulation, and, by selective vasoconstriction of the less important vessels, e.g. of the skin, every effort is made to maintain the oxygen supply on the heart itself. Should the heart for some reason or other be increased in speed, its reserve is appreciably reduced. Also if the heart is affected by some toxic condition its efficiency would similarly be impaired. In such circumstances it cannot respond to any increased demand. Such inefficiency would be brought about by oxygen want itself and this appears to be the case in carbon monoxide (coal gas) poisoning. In this condition not only does the carbon monoxide prevent the hæmoglobin from taking up oxygen,

but it also prevents it from giving up its oxygen to the tissues, including the heart. The latter fails to respond to any increased demand and fainting on the slightest exertion is common.

Adaptation on the part of the circulation is well seen in the anæmias, in which the function of hæmoglobin in a given volume of blood is much reduced. In some varieties, as was shown by Lorrain Smith in relation to chlorosis, the total volume of the blood may be much increased. This latter fact, in conjunction with increased action on the part of the heart, is that which renders chlorotic patients so free from symptoms when at rest, although there may be a complaint of palpitation. The blood carries less oxygen per c.c., but an adequate amount is carried in a given time, as the result of the increased speed of the circulation. Such patients are, however, very breathless on exertion, as the heart cannot respond adequately to further demand and there is, as it were, a relative cardiac failure which results in an inadequacy of the circulation. The mechanism of the production of such breathlessness has already been discussed in relation to "Breathing."

As the result of the anæmia also, carbon dioxide will tend to accumulate in the medullary centres as the result of the supply of an inefficient blood. Not only will inadequate oxygen be carried but insufficient carbon dioxide will be removed, for we now know that the red blood corpuscles play a very appreciable, although indirect part in the carriage of carbon dioxide.

The Blood.—Here also, unless the blood is a primary factor of the failure, there is considerable adaptation, and the power of the blood to carry oxygen may be appreciably increased. Thus it has been found that in congenital heart conditions, the hæmoglobin may be increased as much as 200 per cent. and the blood volume 100 per cent., with a large increase in the red blood corpuscles. Thus is brought about increased oxygen-carrying power. For more immediate requirements, the work of Barcroft and his co-workers has shown that the spleen contains a store of red blood corpuscles which may be utilized. It can readily be shown experimentally that under conditions of oxygen want or carbon dioxide retention there is a marked contraction of this organ. For more prolonged needs the bone marrow is stimulated to produce more corpuscles, as is seen in hæmorrhage or in some of the anæmias where there is a pathological destruction of red cells.

From what we know of the methods by which gases are carried in the blood (*q.v.*) it will be evident that where there is an increased oxygen-carrying power there is also an increased power of carrying carbon dioxide.

The adaptation of the blood is seen in life at high altitudes, indeed it has

been taken advantage of in the training of horses in South America. Attempts were made to train the horses at high levels and when they became adapted to bring them down for racing purposes to the plain as it was found that they had greater staying power. The opposite state of affairs is seen in individuals who lead a sedentary life and who have usually a deficiency in hæmoglobin. It has not been shown that there is any reduction in the breakdown of red blood corpuscles which normally occurs in the liver, etc., but attempts are made to produce this artificially by the inhabitants of Styria where the arsenic eaters are well known. It is considered that the arsenic prevents the corpuscles from being so easily broken down, and, by diminishing the normal destruction of blood corpuscles, increases the oxygen-carrying power of the blood, and, consequently, the efficiency of the individual to do heavy muscular work is increased.

Even if the blood itself is the cause of the failure, there may be a small amount of adaptation on the part of the organs which normally produce blood, and immature nucleated red cells may be thrown into the circulation to assist in the oxygen carriage. There is increased nitrogen metabolism and a diminution in the amount excreted, indicating that new tissue is being formed, while post-mortem examination shows that this actually is the case in the marrow of the bone. The normal yellow marrow of the long bone is converted into red marrow which is a blood-producing tissue.

Liver, Kidney and Intestine.—The adaptation on the part of these organs brings about an increased excretion of acid in combination with ammonia and as acid phosphate, while there is reduction in the amount of alkaline phosphate excreted. These matters are dealt with in relation to body neutrality. In the present connection, however, they are important as they may assist in the elimination of carbon dioxide which may be excreted as carbonate or room may be made for it as it were by the excretion of other acid ions such as chlorides. As the result there is less stimulation of the respiratory centre than would otherwise be and respiratory activity is spared. Thus is maintained a certain amount of pulmonary reserve. The operation of this mechanism is well seen in conditions of inefficiency of the circulation and respiration. Should, however, conversely, the liver be the primary failure, as in acute liver atrophy, or the kidney in nephritis, then the other mechanisms (in the first instance respiration) increase their activities to make up the deficiency. Adaptation on the part of these organs probably accounts for the fact that cases of congenital heart disease, which may be quite cyanosed, are not nearly so breathless as might be expected, nor are often other cases of chronic cardiac conditions. It

is interesting to note that in cases of chronic respiratory difficulty, as in lesions tending to close the larynx where a considerable amount of adaptation has taken place, the sudden relief of the respiration may have disastrous results. It is quite well recognized by laryngologists that after tracheotomy such patients have been found to die for no accountable reason. It appears more than likely that such fatalities are due to an excessive loss of carbon dioxide, the normal method of excreting being added to adaptation on the part of other organs.

It will be observed that the reserve mechanisms which are brought into play are those which are normally brought into action in exercise when extra work is required in regard to gaseous exchange and acid excretion. *These mechanisms have therefore a twofold function in that they are also available should a breakdown occur or as a reserve for increased activities.* It is evident then if a breakdown does occur there is less reserve to spare and we see why an individual who may be quite comfortable at rest may be in intense distress while doing a comparatively small amount of exercise. It will be further realized that tests for effort-tolerance cannot be strictly held to apply to any special system but to all which are responsible for elimination of carbon dioxide and oxygen supply, although in actual practice, after exclusion of other factors, these tests may be of value in estimating cardiac efficiency. The more acute the failure, the more severe the strain on the adaptive mechanisms. In treatment, therefore, it is essential not to delay therapeutic measures since when the limit of adaptation is reached the oxygen want and the carbon dioxide retention themselves intensify the condition, causing especially cardiac enfeeblement and exhaustion of the respiratory centre.

A vicious circle is thus brought about which may rapidly end the life of the patient, the final mode of exit being commonly failure of the heart or respiration. Every effort has to be made then to prevent acute oxygen want and carbon dioxide retention. Propping up of the patient in bed, the giving of cardiac tonics and the administration of oxygen are all of value. Much is also to be said in favour of bleeding to relieve temporarily the right side of the heart when failure of this organ is threatened from any cause whatever. Theoretically, carbon dioxide retention could be counteracted by the administration of sodium bicarbonate or alkaline sodium phosphate, but actually the oxygen want, which commonly occurs at the same time, is the factor which calls for most immediate treatment and the carbon dioxide in stimulating the respiratory centre is of the greatest assistance in improving the oxygen supply. As the subject of oxygen therapy is of especial interest, it is discussed separately (page 173).

RESPIRATORY PROTECTIVE REFLEXES

These reflexes are of the utmost possible importance to the clinician, although of less interest to the physiologist. They are essentially designed for the protection of the lung and are the natural means by which the respiratory tract is cleansed. Dust is continually being inspired but becomes deposited on the ciliated epithelium of the respiratory tract and by means of the ciliary movement is brought up to the pharynx when by a simple movement it is turned over into the œsophagus and swallowed. In inflammatory conditions, however, the mucous membrane may be unduly sensitive and there is increased secretion in an attempt to wash out the irritant. This secretion itself may further act as a foreign body and irritate the mucous membrane. That these secretions and reflexes are protective is commonly recognized, but what is often forgotten is that they are essentially reflexes and as such are liable to exaggeration like all other reflexes.

In *sneezing,* the sensory terminals in the upper respiratory tract are stimulated, and by a complicated mechanism with which we are all familiar, air is suddenly released from the lungs through the nose. The reflex concerns the clinician when it is exaggerated, as it is in chronic nasal conditions, which may or may not be associated with active pathological lesions. In many instances there is simple exaggeration of the reflex with possibly severe "running" of the nose and temporary congestion of the mucous membrane. Although the nasal condition may be important and the starting-point of the abnormal state, too much attention must not be paid to this. Some individuals sneeze every morning on getting up, but that this is really an exaggerated simple reflex or a habit is seen by the fact that the sneezing becomes worse at the end of a university term, when all reflexes tend to become exaggerated, and may disappear entirely during vacations. When the sneezing is accompanied by secretion it may be of considerable discomfort to the patient, but it is evident from what has been said above that local treatment is useless if the general state of the health is not improved. Cocaine sprays or the application of other anæsthetics such as menthol have a deserved reputation in benefiting the condition as they simply paralyse the sensory terminations. The danger of the former, however, is well known in relation to the possible formation of the cocaine habit.

Cough is, however, a more serious matter and the mechanism of its production requires no description. Any part of the respiratory tract is sensitive although the relative sensitivity of different parts may vary. This is seen from the fact that instruments passed down the tract tend to cause coughing, but so

long as the instrument is not being moved the irritation caused appears to be inappreciable. Thus a tracheotomy tube or even a bronchoscope causes little or no irritation when once it is in position. The pleura also is sensitive, a fact to be remembered in tapping a pleural effusion. If the lung is touched with the point of the needle, the latter must be withdrawn, as cough is likely to cause tearing of the lung against the point of the instrument. In the past it has been customary to describe any irritation of the vagus as causing cough. Thus a stomach cough or even a uterine cough has been described. That these may not exist is not dogmatically denied, but we do know that many of the so-called stomach coughs have subsequently been seen to be really pulmonary tuberculosis and that severe stimulation of the vagus in the stomach such as occurs in operations in that organ under local anæsthesia of the abdominal wall only, does not cause coughing nor does gastric irritation sufficient to cause vomiting. What appears to be most likely is that those coughs which cannot be explained on a physical basis, e.g. irritated throat or pulmonary bronchitic condition, are probably habit coughs or exaggerated reflexes and the result of an irritant condition at some previous date. Physiologically this is to be expected from a knowledge of reflexes, and there can be little doubt that this is the explanation of the fact that no fewer than twelve preparations in the pharmacopœia, including the much used Tinct. Camph. Co. and Dover's Powder, designed for the alleviation of cough, contain opium or a derivative which will simply act on the reflex condition. In this light the desirability of stimulating expectorants or of the haphazard doling out of Mist. Expect. Stim. in dispensary work appears to be very doubtful, even if they do give relief in loosening the phlegm. After all, there is a vicious circle, secretion causing cough and cough causing secretion, while the longer the cough persists the more difficult it is to abolish the reflex or reduce it to its normal sensitivity and the more likely is chronic bronchitis to develop. In other words, the reflex nature of the cough must not be lost sight of in an attempt at temporary alleviation and after all in such cases it is the mechanical act of coughing which by increasing the pulmonary resistance and causing failure of the right ventricle, not to speak of the actual damage to lung tissue, which is the real danger to the patient. As yet little attention has been paid to the general state of the patient in relation to the so-called "winter" cough so common in our islands.

Many cases of *asthma* are simply exaggerated reflex phenomena as in chronic bronchitis. As, however, the evidence is that the bronchioles play very little part in the protection of the lungs, their function and their relation to asthma are considered in relation to cyanosis and breathlessness.

Another protective reflex which concerns the clinician is the abolition of abdominal breathing—the classical sign of the acute abdomen. Here the abdominal muscles become rigid in an attempt to protect and prevent movement of underlying viscera and the descent of the diaphragm is prevented. The importance of this reflex lies in its being an aid to diagnosis, but it is obvious that respiration may be seriously affected thereby.

CHAPTER XXI

PHYSIOLOGICAL PRINCIPLES IN FEEDING. BASAL METABOLISM

The body must be considered as primarily designed for the production of work. Like any other machine it must therefore be supplied with fuel, and material for wear and tear. There are certain body processes which require the intake of special ingredients, such as vitamins and salts. At the same time the food has to be in a form suitable for the engine, i.e. it must be suited to the absorptive and digestive mechanisms of the human being, allowing for the very artificial conditions under which he lives.

ENERGY SUPPLY AND TISSUE REPAIR

The intake of fuel is mainly in the form of carbohydrates and fats, and material for repairs as protein. The actual amount required, as in any engine, depends on the amount of work to be done, while the repair necessary is a more constant item, although, as emphasized by Cathcart, the more work, the more wear and tear, and the more protein usage. There are certain vital processes and mechanisms which must be kept going. Even the maintenance of the life of the tissues necessitates a certain expenditure of energy. There is, then, a certain amount of protein necessary under all conditions. This we know as the irreducible protein minimum, and as proteins themselves vary in constitution there will be a minimum of the special proteins which are required as special spare parts. Actually proteins are such complex substances that when all that is required for repair has been utilized, the protein molecule has its nitrogen removed and can be utilized as a source of energy. In the body energy is transformed into a variety of forms, such as muscle movement, secretion and nerve energy, while incidentally a large amount is converted into heat, most of which is useless and is dissipated. Actually only about a fifth of the energy value of the food appears as external work, i.e. muscle work, but even then the body is more efficient than an ordinary steam-engine in which a large amount of energy is dissipated as heat.

All foods have a certain energy value depending on their chemical constitution. This is expressed in terms of large calories, one calorie being the amount of heat required to raise the temperature of one kilogram of water one degree centigrade.

The actual investigation of the calorific value of foods is carried out by burning the substance (in oxygen) in a small steel vessel known as a bomb calorimeter. The vessel is surrounded by a known volume of water which is again enclosed in a non-conductor. Any rise of temperature brought about by the combustion raises the temperature of the water and from the rise thus brought about the calorific value may be calculated. For the main classes of food they are found to be approximately as follows, the values being given as the energy value of 1 gramme of food substance:

Carbohydrate, 4.1 calories; fats, 9.3 calories; proteins, 4.5 calories, but 4.1 in the body.

The energy value of foods burnt in the animal body may be investigated by a somewhat similar experiment in which an animal or man is placed in a chamber where the heat produced can be measured. This kind of experiment gives similar results for carbohydrates and fats, but as protein is incompletely oxidized in the body, the full value (5.0 calories) for the latter is not obtained.

From calculations made in such experiments it is found that a man doing moderate muscular work expends energy to the value of 3,000 to 3,500 calories daily. He must then be supplied with an equal amount of energy. If he lies in bed with only the essential functions of the body to maintain he will only use about 1,700 calories. In the past this conveyed very little to average minds, but since the Great War, rationing has made us more appreciative of food values. When it is considered that the Army ration is one of 4,500 calories, it may readily be realized that the average person consumes a diet which is certainly not deficient. The values of average dietaries are of considerable interest for comparative purposes, and where an attempt is being made to reduce or increase the energy intake. In this connection I am indebted to Dr. R. D. Lawrence who worked out the values of average dietaries for this purpose. They are given at the end of the chapter.

The amount of energy expended at rest is remarkably constant in the same individual from day to day, although it may vary over longer periods depending on the conditions of life. This is known as the *basal metabolic rate, or basal metabolism.* For comparative purposes it is expressed in terms of the calories expended per square foot of body surface. Of recent years the subject has become one of considerable clinical importance, for in many diseased conditions it may be of value as an aid to diagnosis and treatment. Special methods by which the heat value can be calculated indirectly are now in extensive use. A fuller consideration of the subject is given later on page 191.

Much interest has centred in the protein constituents of the diet. It is

the most expensive part of a diet, and the condition of high blood pressure in adults appears to be associated with it. It is possible to exist on about one-third of the amount of protein usually taken. Compared with carbohydrates and fats, protein requires much more work to be done on the part of certain organs, especially the liver and kidney, and it seems possible that these may become overtaxed.

We have seen that there is an irreducible protein minimum, which depends on the source of the protein. This minimum is less for meat protein than for that derived from vegetables. This is due to the different amount and nature of the amino-acids of which they are composed. Certain amino-acids, such as tryptophane, are essential to life, and from what we know of the chemical constitution of some of the internal secretions (thyroid and adrenals), it appears likely that these amino-acids are necessary for their formation. Special ones are required for the young growing animal, but in adults this does not seem to be so essential, for they have acquired the facility of forming the special amino-acids from their food. For young persons, therefore, no attempt should be made to limit the source of protein. It is to be expected that those which contain most of the necessary amino-acids for the formation of new tissue and blood are of the greatest value. Meat, milk and eggs head the list, as being the most generally useful, or, as we may say, have the greatest *biological value.*

Protein has a special property in that it stimulates metabolism. It has been noted that people on a reduced protein diet feel cold, and that the inhabitants of colder climates are almost invariably protein eaters. It must not, however, be forgotten that with the meat there is always some associated fat which has a high calorific value. Moreover, the fat "burns in the fire of the carbohydrates," and we may look upon the proteins as fanning the flame. If a man is fed almost exclusively on moderate amounts of protein and vegetables (which have but little carbohydrate content) his appetite will be satisfied, but the heat value may be insufficient for his requirements. Further, even at rest, his metabolism will be stimulated by the protein. He will therefore use up his own stores of energy and become thin. This is the basis of many forms of treatment for obesity.

If very large quantities of protein are consumed the object of the treatment will be defeated, for the heat value of protein (in the body) is equal to that of carbohydrate. If the amino-acids which result from protein digestion are not required, they are de-aminized and used as fuel. It is notorious that certain individuals become fat on a comparatively low diet. It can only be assumed

that such people can carry out work, *if* they work adequately at all, with a minimum expenditure of energy.

As yet we are still in difficulty regarding the amount of protein the diet should contain. On the one hand, we have (as pointed out by Leathes) evidence that an infant, even allowing for its growth, takes ten times that which might be regarded as its normal protein requirement. On the other hand, it is known that many who have a high blood pressure can get it reduced if their protein intake is reduced. This may be the result of lessened strain on organs such as the kidney, or due to toxic substances which cause vaso-constriction, or from the additional supply of depressor substances from the vegetable diet which usually replaces meat. It is accepted that those who take insufficient protein appear to be less capable of withstanding infection and are generally less robust. Halliburton suggests that so-called stamina or reserve force may be dependent on protein and more recently J. W. Macleod has drawn attention to the decided inhibitory action which certain amino-acids may have on the growth of bacteria. While this may be so, it is certain that those suffering from illness or building up new tissue require additional protein, as evidenced by the fact that their nitrogen excretion is reduced. Here may be repeated the time-honoured warning against beef and chicken tea which have gained such a reputation in the popular mind. In such decoctions the protein is coagulated in the boiling and falls to the bottom and the tea, although no doubt deliciously tasty, is about as valuable as the water in which an egg is boiled so far as nourishment is concerned! It is, however, a valuable stimulant of appetite and of digestive secretion and may be a convenient vehicle by which nourishment may be conveyed when the appetite is flagging.

For individuals doing very hard muscular work, as emphasized by Starling, fat is an essential part of the diet just as it is for those who live in the Arctic Regions and have enormous heat loss. When the energy expended is large the necessary intake cannot be readily obtained in carbohydrates, as these in excess become distasteful. Fat with its high calorific value of 9.3 is a concentrated form in which energy may be taken, and if it is not supplied the desire for fat may become a real craving.

At the same time, although we have said the carbohydrate is essentially fuel and may be much reduced, it cannot be entirely replaced by fat. Just as fat is not readily inflammable in the ordinary sense unless it is associated with other combustible material, so also in the body fat requires a more readily oxidizable substance to be burnt with it. The formula of a carbohydrate, e.g. $C_6 H_{12} O_6$, indicates that it contains sufficient oxygen to oxidize all its hydrogen

to water, and that oxygen is needed for the carbon. Fats, on the other hand, e.g. palmitic acid, C_{16} H_{49} O_2, or tripalmitin, C_{49} H_{36} O_2, require oxygen not only for their carbon, but also for the hydrogen before the fat is wholly converted into carbon dioxide and water. Hence, in the burning of carbohydrates, the volume of carbon dioxide produced is equal to that of the oxygen taken in. The **respiratory quotient** (R.Q.), i.e. the ratio

$$\frac{\text{volume of carbon dioxide given out}}{\text{volume of oxygen taken in}} \text{ is 1.0,}$$

whereas in the case of fat the value is 0.7. Here a certain amount of oxygen is got rid of, not as carbon dioxide, but as water. It is evident that the R.Q. will be an index as to the amount of carbohydrate being burnt as compared with fat. On a mixed diet the R.Q. is 0.8 to 0.9, whereas in diabetes (where there is reduction of carbohydrate metabolism) the R.Q. is much reduced. On the other hand, in exercise, when a greater proportion of carbohydrate is used, the normal person has a slightly raised R.Q.

The Vitamin Content of Food.—Work of recent years has shown that many of the properties previously assigned to meat really depend on the accessory food factors it contains. For example, in the Japanese Navy it used to be thought that meat was of special value in warding off beriberi. This disease we now know is due to vitamin deficiency. We can look upon the vitamin content as constituting the essential freshness of the diet and so important has this problem now become that a discussion is deferred to a subsequent chapter.

The Suitability of the Food for the Alimentary Canal.—Undoubtedly many of the ailments of everyday life are the result of failure to recognize the importance of this factor. Food must not only be of a certain chemical constitution but it must be appetizing and have a considerable indigestible bulk. The more physiologists study the subject the more it is realized that food taken without relish takes longer to be digested. The nervous influences in alimentary secretion (see page 221) are very great and, as the result of the stress of our so-called civilization, too often ignored.

Further, the physical state of the food is of enormous importance. For example, the taking of fluid carbohydrates has much to condemn it, although the practice is common, and if this is combined with the fact that the food contains little or no indigestible material, the condition is serious. In this respect specially refined cereals, such as those which constitute milk puddings, are to be heartily condemned. From what we know of the mechanism of ptyalin indigestion we believe that carbohydrates should be taken reasonably dry in order

that they may be mixed thoroughly with saliva and in order that the ptyalin digestion can be adequately continued in the stomach.

If the food has insufficient bulk the difficulty of the gut in driving it on may be compared with that of trying to climb a thin steel wire. This would be extremely difficult, for a proper grip cannot be obtained, whereas if the wire were replaced by a thick rope the matter is easy. The beneficial effects of vegetables and fruits depend largely on the fact that the cellulose they contain remains undigested. Under modern conditions the problem of the supply of such articles of diet at a reasonable cost in winter is no easy one. These substances are also of great value, because of their vitamin content. Many of the benefits of porridge made with coarse oatmeal lies in the large amount of indigestible material associated with its high protein, salt, and carbohydrate content. Its general value is added to by the milk taken at the same time. Refined carbohydrates should then be taken in association with as much cellulose as possible. If milk puddings must be taken they should be accompanied with fruit if possible. Coarse bread should be preferred to the finer varieties. Cooking has the advantage that it permits digestive enzymes to penetrate better. The diet of the ordinary person is usually in excess of his requirements, and the taking of food in its natural state, though it may be wasteful, has much to commend it (provided it is not too irritant to pass the pylorus), for the undigested parts add much to its bulk. This matter is discussed further in relation to the movements of the intestine.

The physical state of the food also plays a considerable part in the production of dental decay. If a tooth is disused by removal of opposing one, it too tends to degenerate. In like manner if we take food for which the teeth as a whole are not required a similar result will occur. This is further facilitated by the fact that the more bland starchy foods which do not require chewing, tend to reduce the stimulation of saliva. Sims Wallace has pointed out what a large part the saliva plays in the cleansing of the mouth, and the prevention of fermentable food deposits around the teeth.

Sunlight.—It is a familiar fact that persons, especially children, are in better health if they live to a large extent in the open air. Particularly has this been impressed upon us by the recent results of the investigations into rickets, which, it has been pointed out by McCarrison, is more common in the poorer classes in this country, but in the better classes in India. The subject is dealt with in more detail in the chapter on "Vitamins," but here it may be stated that it has now been conclusively shown that if the individual is exposed to light the vitamin content of his diet need not be so high. Some of the older authors used

to consider it a possibility that the body actually received energy from the sun. It may be that this is an approximation to a truth after all, and in any case in many pathological conditions, e.g. rickets and tuberculosis, sunlight has an undoubtedly beneficial effect. The general experience of the War and of native races suggests that sunlight may play an important part in the production of resistance against bacterial invasion.

Water and Salts.—The water or fluid intake per day should be at least 100 ounces, to permit of a satisfactory allowance to all the organs. Note here that fruit and vegetables contain over 90 per cent. of water. A large amount of constipation is due to an inadequate fluid supply, and various urinary deposits similarly result from the formation of a too concentrated urine. The water supply of the body is considered more fully later.

The salt content of the diet is usually left to look after itself, since the ordinary foods contain an abundance of those necessary. Pathological conditions teach us that the salt supply cannot altogether be neglected. Goitre has now been shown to be the result of iodine deficiency (see page 202). This salt occurs in many of the common articles of diet, such as onions, carrots and eggs. In chlorosis the beneficial effects of iron indicate that it is an essential part of the diet, as might have been expected from the composition of hæmoglobin and the excretion of bile. Phosphates are concerned in the maintenance of body neutrality. They appear also to play an important part as stimulants of intestinal movements. It should also be noted that though iodine and iron may be supplied in sufficient quantity, they may not be absorbed. This may be the result of intestinal conditions, and it is only when the latter are treated that the apparent deficiency is made up. In certain circumstances some salts, such as those of calcium, are more important during growth than others.

The absolute necessity of sodium, potassium, and calcium is seen in their effect on the heart-beat, in the contraction of smooth muscle. The mammalian heart or a strip of gut can be affected by these ions when isolated from the body. In the case of the intestine a trace of magnesium also appears to be beneficial. No definite deficiencies in these salts have as yet been described, except in the case of calcium. According to Vines there is a definite lack of calcium in parathyroid deficiency, which may result in tetany. The work of Vines in this respect has not yet been reconciled with that of Noël Paton, who has given evidence that the tetany of parathyroid deficiency is the result of a deficient guanidine metabolism, but from the recent work of Collip it would seem that the reconciliation of the two views is not far distant.

The desirability of varying the sodium chloride content is dealt with in relation to the water content of the body.

BASAL METABOLISM

Basal metabolism, or the basal metabolic rate (B.M.R.), has recently been brought into prominence as a factor of much clinical value. It is the heat expended by the body at rest, and in circumstances under which it is doing a minimum of work, all functions being reduced accordingly. There must also be a state of mental quietude, often difficult to obtain in nervous patients, for whom mental rest can only be attained by accustoming them to the procedures necessary. For details of the method of finding the B.M.R. reference must be made to practical works; the general principles only are here indicated. The energy expended is theoretically best ascertained by placing the patient in a calorimeter, but obviously this is impossible in practice, and indirect methods must therefore be used. In these the oxygen consumption is measured, and from the relative amounts of carbohydrates, fats, and proteins oxidized, the number of calories may be calculated. The common method in this country is to collect the patient's expired air for ten minutes, in a spirometer or a Douglas bag. The latter is an air-tight bag of about 50 litres capacity, and used in connection with a valved mouthpiece. From an analysis of the inspired air and expired air the amount of oxygen used during that period can be obtained. From the amount of nitrogen in the urine, the oxygen used in consuming the protein can be calculated. The remainder is used in the oxidation of carbohydrates and fats, the relative proportions of which are indicated by the respiratory quotient. Knowing the heat value of these foods we can calculate the number of calories produced per litre of oxygen used. Having already found the amount of oxygen used in a given time, we can determine the total number of calories expended in that time.

Apart from some experience of gas analysis which is not difficult to obtain, no special technical experience is required and much calculation is avoided by the use of tables.

It is obvious that an individual with a low metabolic rate is one who requires less energy supply for his essential functions and he will, therefore, have more to spare for other work. If the excess is not used in such work there will be a tendency to grow fat, and similarly those with a high metabolic rate tend to become thin. As would be expected, febrile conditions raise the basal metabolism provided the reserves of the body are not exhausted from long illness, and various attempts have been made to use this as an aid in the diagnosis of

obscure conditions, e.g. tuberculosis, whether the patient is febrile or not, and so on. It is clear, however, that in such conditions the basal metabolism will depend on the actual state of the individual patient. Obviously, too, the taking of a large protein meal will increase the B.M.R. in view of the specific dynamic action of protein, and for purposes of comparison the desirability of making observations before breakfast is seen.

In certain conditions there is a definite stimulation of metabolism and particularly is this now the case in hyperthyroidism in which the B.M.R. is a usual method of differentiating nervous conditions from those thyroid cases in which the exophthalmos is not developed. Further, the B.M.R. is a very definite indication of the efficacy of treatment (page 204), and is a routine measure in modern scientific investigation. In myxœdema there is a corresponding diminution in metabolism and the tendency of such individuals to put on fat is well known.

A little difficulty exists in finding a really accurate method for expressing the results for purposes of comparison. We have said for an average adult the basal metabolism was about 1,700 calories per day. The energy output is commonly expressed in terms of body surface, the surface being calculated from the height and weight, but others prefer to express the result as a percentage increase or decrease on the normal, the normal being considered 40 calories per hour per square metre of surface.

It will, however, be realized that the surface of a very large individual may not depend on an increase of active tissue but on fat, and for very active work Benedict has constructed elaborate tables which give the standard metabolic rates for a variety of persons of different size, age, weight, and sex. The latter is necessary, as men have a slightly higher rate than women.

The nervous system has also a marked influence on metabolism. We are all familiar with the highly-strung neurasthenic individual who is thin although he may take large supplies of food. In such an individual the reflexes are exaggerated and the increase in tone uses up more energy, while he expends more energy in maintaining the essential functions. It is also noticed that such individuals have not infrequently a decided liking for proteins and highly flavoured articles of diet and may have even a disgust of fats. This dietetic selection may further contribute to their thinness in accordance with what has been said above. The opposite effect is evident in the imperturbable happy and rotund individual who seldom gets flurried. Such a mental state added to excellent digestion, which act beneficially on each other, forms a good physiological basis for the truth of the old adage: "Laugh and grow fat." Other than the thyroid

mentioned above there is evidence that basal metabolism may be affected by several of the internal secretions. This is dealt with further in a succeeding chapter.

THE FOOD AND CALORIFIC CONSUMPTION OF THREE NORMAL INDIVIDUALS

By R. D. LAWRENCE, M.A., M.D., Chemical Pathologist,
King's College Hospital

The study of dietetics is a science of its own and has little to do with the control of our eating. Our eating is mostly an instinct, perhaps partly an art, controlled by our appetites and our purses. Not even the dietetic expert chooses and eats his food in terms of calories. But the relation between the two is close and interesting, and, in the study and control of certain diseases such as diabetes and obesity, of great importance.

To give an idea of the exact relation of calories to the food eaten by the normal promptings of appetite, the average diet for the day of three individuals is recorded below in detail. Although only one day is recorded, other days were observed and it is felt that the day's diet is fairly representative. No restraint was put upon the amount of food eaten. They helped themselves or asked for second helpings if desired and the food was weighed afterwards. The food values used are taken from the Food Tables of Harrison and Lawrence and, although it is somewhat difficult to compute the exact composition of mince pies and treacle cake, the calorific values and weights are as accurate as is ever practicable.

The main object being to show in practical detail the relation between the food eaten and its calorific value and content in carbohydrate, protein and fat, no special attempt was made to study a perfectly average eater. Indeed, one large eater and one light were purposely chosen to provide a contrast. It is well known that the calorific requirements of the average young male adult, leading mostly a sedentary student's life, as these three examples were doing, is usually from 30 to 40 calories per kilogram of body weight and it will be seen that the heavy and light eaters fall respectively above and below this average, while the third is normal. All three are English and a few details as to weight and obesity, etc., are given in each case. It will be seen that the lightest eater is the only one who is at all obese, but it is not clear that this relation of input to output has always been the same.

Case A, aged 25; height, 5 ft. 11 in.; weight, 11 st. 4 lb. (71.6 kilograms). Average weight for height is 10 st. 13 lb., so that he is slightly above weight; habits not active except that he usually bicycles about 10 miles a day; noticeably a *big eater.*

Food	Weight in Ounces	Food Content in Grams		
		C.	*P.*	*F.*
Breakfast				
Porridge	10½	35	7	7
Sugar	1	30	0	0
Kipper	1½	0	8	3
Butter	1	0	0	25
Toast	2¼	45	4	0
Marmalade	1⅛	27	0	0
Milk	3	5	4	4
		142	23	39
Lunch				
Roll, bread	1	15	3	0
Sausage	1½	1	5	12
Potato	4	27	3	0
2 Apples	10	32	1	1
		75	12	13
Tea				
2 Biscuits	1	20	4	0
Milk	2	3	2	2
		23	6	2
Dinner				
Soup, thick	3½	6	3	2
Steak	7	0	52	26
Pudding	2½	28	3	3
Onions	8¼	11	2	3
Potato	7½	50	5	0
Bread	1	15	3	3
Stewed Fruit	4	15	2	0
Custard	2½	17	4	4
Sugar	½	15	0	0
		157	74	41
Supper				
Treacle Cake	6	120	3	10
Day's Total	.....	517	118	105
Calories	.....	2,068	472	945

Total Calories = 3,485.
Weight = 71.6 kgm.
= 48.7 calories per kgm. of body weight.

Case B, aged 35; height, 5 ft. 2½ in.; weight, 9 st. 10 lb. (61.6 kgm.). Average weight for height is 8 st. 8 lb., so that he is above the average weight and is noticeably obese; active and quick in his movements, but takes no exercise, not even walking; noticeably a *small eater;* has a distaste for fat and butter; probably partly restricts his food to avoid obesity.

Food	Weight in Ounces	Food Content in Grams		
		C.	*P.*	*F.*
Breakfast				
Bacon, lean	½	0	5	5
Potato	1	6	1	0
Toast	¾	15	3	0
Marmalade	1	25	0	0
		46	9	5
Lunch				
2 Crumpets	2	30	6	0
Butter, 2 pats	½	0	0	12
Mince Pie	—	20	4	5
Jam Tartlet	—	25	4	0
		75	14	17
Tea				
2 Rock Cakes	1½	22	4	4
Dinner				
Soup, thick	3¼	6	3	2
Steak	3	0	22	11
Pudding	1½	17	2	2
Onions	4¼	6	1	2
Stewed Fruit	7½	28	3	0
		57	31	17
Supper				
2 Biscuits	1	20	4	2
Total for Day	.....	220	62	45
Calories	.....	880	248	405

Total Calories = 1,533.
Weight = 59 kgm.
= 25 calories per kgm. of body weight.

If we calculate his calorific usage on the average weight, which is more correct in some ways, as his "extra" fat is not metabolically active tissue, then we get the figure of 29 cals. per kgm. of body weight.

Case C, aged 24; height, 5 ft. 11 in.; weight, 9 st. 4 lb. (59 kgm.). Average weight for height is 10 st. 13 lb., so that he is considerably under weight and is quite thin; he is active and plays games occasionally, but not daily; eats slightly less than the average student.

Food	Weight in Ounces	Food Content in Grams		
		C.	*P.*	*F.*
Breakfast				
Porridge	5	16	3	3
Milk	5	7	5	5
Sugar	½	15	0	0
Bacon	½	0	3	8
Potato, fried	2¾	20	2	5
Toast	1	20	4	0
Butter	¼	0	0	6
Marmalade	¾	19	0	0
		97	17	27
Lunch				
One Sausage	—	1	5	12
Potato	6	40	4	0
Brussels Sprouts	4	4	2	0
1 slice Jam Roll	—	25	1	0
		70	12	12
Tea				
1 Banbury Cake	—	20	4	0
Milk	½	1	0	0
		21	4	0
Dinner				
Soup, thick	5¼	8	4	3
Steak	3	0	22	11
Pudding	1	12	1	1
Potato	3	20	2	0
Onions	2	3	0	1
Stewed Fruit	4	15	2	0
Custard	1½	10	3	3
Milk	3½	5	3	3
		73	37	22
Total for Day		261	70	61
Calories		1,044	280	549

Total Calories = 1,873.
Weight = 59 kgm.
= 32 calories per kgm. of body weight.

CHAPTER XXII

VITAMINS

We have seen that vitamins may be considered as the essential freshness of food, but nearer than that we cannot get, for their chemical nature is unknown. Further, the amounts of these substances which we require are infinitesimally small. We know, however, that they are essential to life and although in the past their supply has offered little difficulty, with the increasing congregation in towns this supply will be a more important problem. And there can be little doubt that many of the old adages regarding the eating of fruit and vegetables depend for their truth on the fact that these articles contain vitamins and at the same time stimulate the movements of the intestinal contents in virtue of their indigestible bulk.

We know of four classes of vitamins which non-committally are called "A," "B," "C" and "D." "A" and "D" are fat soluble, the other two water soluble.

Vitamin "A" and the Anti-rachitic Food Factor (Vitamin "D").—These vitamins are of peculiar importance in this country and a great deal of controversy has raged around them especially in their relation to rickets, but it is now clear that the former vitamin, which is essential for growth, is not identical with the anti-rachitic vitamin as was first thought. For practical purposes, however, the anti-rachitic vitamin "D" is so like vitamin "A" in its distribution and properties that they may be considered together. Of recent years two distinct views have been put forward regarding the ætiology of rickets. One, the Glasgow School, headed by Noël Paton and Findlay, which stressed the importance of general hygiene, and the Cambridge and Sheffield Schools, headed by Hopkins and Mellanby, which laid chief importance on diet, and so resuscitated some earlier theories. Happily, the views of each are now being blended and an honourable peace appears to have been almost reached.

Source:—These vitamins are synthetized by all living chlorophyll-containing plants. Should the plant have no chlorophyll, e.g. a mushroom or a seedling grown in the dark, it has no vitamin. From this source the vitamin is obtained by animals directly or indirectly. As we have seen, it is soluble in fat and is contained in animal fat provided the animal has itself taken in this vitamin.

Thus the milk of a cow may contain much vitamin "A" when on the grass, but this is much reduced or may be entirely absent in winter if the cow is fed on artificial food. The same is true of butter. Animals such as fishes whose fat contains much vitamin, e.g. cod-liver oil, obtain it from the green algæ or the chlorophyll-containing organisms of the "plankton." Vegetable fats, on the other hand, which are made from seeds, curiously enough contain no vitamin with the exception of palm-oil which is unfortunately most unpalatable. It is evident, then, that the vitamin will be deficient in the cheaper margarines made from vegetable oils. Normally we take our vitamins in green vegetables, fruits, butter, milk, animal fats and egg yolk. But in the poorer classes it is evident that these articles may be difficult to procure and their diets are often lacking in this respect.

Unfortunately, too, the vitamin can be destroyed by heat in the presence of oxygen, but this does not occur completely unless the heat is prolonged and in many instances unless actual steps are taken to destroy the vitamin. Butter may be raised to 130° C. without losing much of its vitamin "A" provided it is not aerated and in the ordinary cooking of vegetables a fair proportion of their vitamin "A" appears to be retained. Milk, on the other hand, is particularly liable to lose its vitamin even in pasteurization, and if sterilization is necessary additional vitamin must be added. The drying of milk on the other hand by the roller process does not appear to be so destructive and similarly tinned meat which is not heated for any prolonged period retains a larger proportion of vitamin in its fat.

Evidence of Vitamin "A" Deficiency.—This deficiency is best seen in puppies and in children in whom failure to grow soon becomes evident. The bones are soft from deficient calcification and readily bend, while there is typical swelling at the epiphyses. There is also marked general weakness as the result of muscle changes, of which the great increase in the creatinine content is the best known. In experimental work, also, it is seen that the animals are less capable of withstanding bacterial invasion and are particularly liable to conjunctivitis. There is also marked malformation of the teeth. The deficiency, it is now clear, may not necessarily be in the diet, but several factors may conspire to bring about what is apparently a deficiency in the absorption or antagonism of the active vitamin. On the other hand, other factors may assist the action of the vitamin.

Sunlight.—Here the two schools of thought have particularly been brought into harmony and it may be summarized that the less sunlight the animal obtains the more vitamin, especially "D," is necessary in its dietary and *vice*

versa. Many of the conditions previously included under the heading of general hygiene undoubtedly depend on the benefits of light. This is explained by the fact that while in this country rickets is a disease of the poorer classes, in India it is a disease of the richer classes whose children, particularly the girls, are kept much indoors. In the same way it can be shown that the milk of a cow kept in sunlight is richer in vitamin than one kept in a dark byre. By exposing animals and substances to ultra-violet light it has also been quite conclusively proved that the light can cause the production of vitamin "D" in the animal, possibly in the cholesterol (which is activated in vitro).

Calcium.—The softness of the bones, it is obvious, is a result of deficient calcification and it is evident that if the calcium of the diet is reduced no amount of vitamin will make up for this deficiency. Thus we see that butter alone, which does not contain the calcium of the milk, is not nearly so good an anti-rachitic as cod-liver oil and if the best effects are to be got from butter therapy calcium in the form of calcium carbonate should be added to the diet. The calcium may not actually be deficient in the diet, but it may not be absorbed, and it has been suggested by Dodds that this result may in some instances occur as the result of pancreatic disorders and the subsequent poor production of fatty acid and poor absorption of calcium. Phosphorus metabolism is closely related to calcium in this respect, but in the present state of our knowledge it is impossible for any definite statements to be made.

Exercise.—It is difficult to separate this factor from the effect of light, but evidence points to this also being important, and, after all, this is what would be expected, as we know that exercise of any part is a stimulus to greater power of function. It is to be expected, then, that greater work on the part of the muscle will stimulate more rigidity in the bones.

Carbohydrates.—That rickets is particularly marked in children whose diets contain an excess of carbohydrates has long been recognized by clinicians, and there is now evidence that carbohydrates inhibit the anti-rachitic vitamin. How this occurs is not certain as yet and meantime can be best understood by the assumption that the carbohydrates contain a specific antagonistic substance. Mellanby has found that certain cereals are more potent than others in this respect and that oatmeal is particularly so. Dwellers north of the Tweed need not be alarmed as normally additional vitamin "A" in the milk is taken at the same time as porridge. The inhibition can, however, be counteracted by increasing the vitamin content of the food.

Vitamin "A" and "D" Therapy.—Here let it be said at once that no proprietary preparation has yet been found to contain so much vitamin as the natu-

ral products, cod-liver oil and whole milk from grass-fed cows. Butter, as we have seen, requires the addition of calcium to get the best effects. The results of vitamin therapy have been most brilliant and do much to confirm the hitherto much criticized vitamin theory of the origin of rickets. The therapy carried out by Chick, Hume and others in Vienna has convinced some of the most hardened sceptics, and when combined with light supplied either from the sun, from a mercury vapour lamp or an arc, there can be no doubt as to its efficiency in the treatment of rickets. A common disease in children is what is known as fat dyspepsia characterized by pale crumbly or soapy stools, and in which the reduction of the fat intake is indicated. It must not then be forgotten in the treatment of this condition that there is a point below which the fat content of the food cannot be reduced unless it is replaced by other vitamin-containing substances without detriment to the patient.

Vitamins "B" and "C."—To the average practitioner these vitamins appear of less serious moment as the classical diseases which result from their deficiency, namely, beriberi and scurvy, are comparatively rare. There is, however, evidence that many of the indefinite malaises and dyspepsias of adult life may be in part due to their deficiency.

Vitamin "B" is contained in seeds, such as the grain of cereals, in fruit, egg yolk and meat. It can, therefore, be stored in the dry state in wholemeal flour and unpolished rice. The vitamin, however, appears to be quite close to the surface as the more the grain is milled or the rice polished the more vitamin is lost. It also can withstand ordinary cooking. Commonly this vitamin is referred to as the anti-neuritic vitamin since its absence brings about conditions in which polyneuritis is the characteristic feature, as in beriberi. This was one of the first diseases shown to be due to dietetic deficiency. Clinically, it manifests itself as a neuritis, with the typical pain, anæsthesia, and it may be wasting and paralysis. In some varieties there is œdema. Actually, however, severe beriberi is very rare, even in those individuals who habitually take only whitened flour. It is to be presumed that they take sufficient vitamin "B" in other ways.

Vitamin "C."—In distribution this vitamin is like the vitamin "A" except that it is not fat soluble and is present in fruits as well as in green plants. In times past the disease scurvy caused by its deficiency was the scourge of ships and prisons, but experience in the Navy at some stations where fresh fruit was available led to the use of lemon-juice as a prophylactic. A mistaken idea, however, that lime-juice being more acid would be more powerful in this respect, led to the adoption of the latter as a regular ration. We now know that the juice of fresh oranges, lemons, swede turnips and cabbages contain more of this

vitamin than other substances, although it is present to a lesser degree in all green plants. Unfortunately it is the least stable vitamin and is extremely easily destroyed by heat. Only a trace remains in vegetables after cooking. It is evident that the best way to obtain this vitamin is in eating of fresh fruit, oranges and lemons for preference; a small amount is contained in meat and milk.

Deficiency of this vitamin brings about the typical scurvy which is seen in the swelling of the gums, loosening of the teeth with a tendency to hæmorrhage and fracturing of bones.

It is especially interesting to note that in the cooking of acid fruits the vitamin is not lost and the same refers to the manufacture of tinned acid fruits. The cooking of vegetables and meat, however, in alkaline solutions is very destructive.

In the foregoing, special stress has been laid on the signs of the deficiency in adults, but it must not be forgotten that the absence of "B" and "C" interferes with normal growth and the vitamin content of milk in the young is of special importance. The attempts to render milk approximately sterile reduces the vitamin and may entirely destroy vitamin "C." Pasteurization is even worse than boiling for a short period. On the other hand, the giving of extra vitamins when the food already contains a normal amount can serve no useful purpose. When vitamins must be given this may be done conveniently—"A" and "D" by cod-liver oil, "B" by yeast extract, "C" by orange and lemon juice.

The efficiency of light therapy does much to consolidate our knowledge of the subject. Here again is the too-often ignored lesson to be learned that although scientific controversy is stimulating in that it builds up a pile of facts on each side, nothing is to be gained by one side attempting to ignore the results of the other. The true solution is found from all the facts.

Of peculiar interest for the future is the fact that all animals must have light or something which is produced by light and if they cannot obtain this directly from the sun they must obtain it indirectly through the agency of plants.

CHAPTER XXIII

THE THYROID

The thyroid, lying as it does around the upper rings of the trachea, and extending upwards and downwards on each side, and covering with its lateral lobes a part of the thyroid cartilage, is largely responsible for the rounded contour of the neck. Changes in its size may be readily noted and this special feature considerably affected the old ideas concerning its functions. It was thought, even by Wharton, to play a part in the mellowing of the voice, and in beautifying the neck of woman in whom it is the more prominent.

We have now clear evidence that it elaborates a "catalyst" which hastens the fundamental reactions of metabolism, and thereby confers on the adult individual a greater range of activity than would otherwise be possible. The truth of this is seen by observing the limitations placed upon those suffering from severe myxœdema or exophthalmic goitre. In the young it is also clear that the thyroid is largely responsible for growth (*q.v.*).

The exact nature of the substance elaborated by the thyroid gland and passed into the blood-stream for long escaped elucidation largely because we were not possessed of methods of determining small quantities of iodine. That the thyroid gland substance contained iodine was shown long ago, about 1895, by Bauman. The active principle of the gland has now been isolated by Kendal, and shown to be an iodized amine to which the name "thyroxin" has been given, although it may be that this is not the only active substance in the gland. The chemical constitution of thyroxin appears to indicate that it may be derived from an amino-acid such as tyrosine formed from the digestion of protein. It is interesting to note that certain of such acids have been shown by Hopkins to be essential to life, especially in young animals (see page 186). It is possible that this relationship to amino-acid may not be unimportant; indeed Kendal believes that it is the NH_2COOH (amino-acid) group in the thyroxin which is the active one, although he has not yet demonstrated its activity apart from iodine. We have already seen that amino-acids are themselves great stimulants of metabolism and it is stated too that thyroxin is appreciably more active if administered along with amino-acids.

The above gives a key to the essential factors necessary in the normal func-

tion of the thyroid gland and indicate clearly the importance of the iodine and protein supply of the body. Here, too, we may remind ourselves that the most advanced nations of the world are the greatest protein eaters and we have already noted the greater sphere of activity which a wide range of metabolic rate will confer.

Protein supply is seldom lacking and we know that adult animals may synthetize special amino-acids, although this is not possible in the young. So far as the writer is aware, no attempt has been made to associate the condition of myxœdema or hypothyroidism with deficient supply of iodine or, more particularly, of protein, but obviously there are possibilities in this direction. Myxœdema is characterized by the evidence of slowed metabolism. As would be expected where there is a slowed metabolism, all the body functions are slow. The pulse rate is low, the mind is dull and response sluggish, while there is a great tendency to the deposition of fat. The skin is dry and the hair thinned, if not lost. The characteristic sign, however, from which the condition receives its name is the myxœdematous degeneration of the subcutaneous tissue already referred to.

Iodine.—Attention has of late been greatly focussed on the iodine supply of the body in relation to the thyroid. Normally we obtain our iodine from articles of diet, such as fish, milk, eggs, certain cereals and vegetables, and we require such small quantities that we need not worry about them, although this does not appear to be so in certain districts of America where the iodine in the soil is low.

Iodine deficiency has now been shown, especially as the result of Marine and his co-workers, to be responsible for the production of simple goitre, a condition in which the thyroid gland is enlarged but which is not associated necessarily with any symptoms other than those due to local pressure. The accumulation of abnormal colloid in the vesicles of the gland is now looked upon as a secondary change analogous to the occurrence of colloidal degeneration in other conditions, although in some instances it may be due to retention. In simple iodine deficiency the colloidal degeneration is preceded by a proliferation of the glandular elements. In districts in which goitre is endemic amongst human beings or domestic animals such as sheep, the administration of iodine has been of enormous benefit. In some instances potassium iodide has been administered to school children on a large scale with most satisfactory results, while in Michigan iodine, administered in conjunction with rock salt, has made sheep rearing possible.

For some time there was difficulty in reconciling with the above the striking

evidence of McCarrison as to the infectivity of goitre as a water-borne disease. This had been corroborated in many quarters. It has now been realized, however, that iodine, like iron, must not only be supplied, but it must be absorbed, and many factors may interfere with its absorption and utilization. These factors have been worked out experimentally, especially by McCarrison, and the results support clinical experience. The absorption may be interfered with by certain intestinal bacteria, and iodine deficiency so produced is common apparently in this country and more so in India where the conditions for the spread of water-borne disease are more favourable. It has been shown that such cases benefit not only by treatment with intestinal antiseptics, such as thymol, but also with iodine and preferably with both. The benefits which accrue from the administration of antiseptics indicate the bacterial factor associated with the disease, even in sporadic cases in this country, although why the condition remains sporadic is difficult to understand.

Excessive Calcium in the diet brings about a somewhat similar interference, and this is considered to bring about the endemic goitre which is associated with Derbyshire. The excessive calcium, according to McCarrison, increases the viscosity of the normal colloid of the gland and favours its accumulation, while an additional supply of iodine counteracts this effect, although unfortunately an abnormal amount of colloid may still be maintained in the gland, as the normal storehouse for iodine is in the thyroid, as is shown by the effect of thyroid feeding.

Certain fats also, especially butter, and the unsaturated oleic acid have been shown to cause goitre in animals, but the ways in which this must be brought about are very numerous and it is by no means clear how they act, although it seems most probable that they combine with the iodine and somehow prevent its utilization.

Hyperthyroidism.—Of more serious consequence is hyperthyroidism in which there is excessive or abnormal action of the thyroid gland. Hyperthyroidism exists clinically in many different degrees. It is characterized by all the signs of excessive metabolism, and excessive sympathetic activity. The heart rate is extremely rapid, the nervous system responds extremely rapidly to stimuli, the skin sweats, the pupils are dilated, and the patient in general appears to be in a very nervous and excited state. In the severer variety there is exophthalmos or protrusion of the eyeballs. Unfortunately laboratory evidence is wanting of an increased secretion of thyroid in exophthalmic goitre. There is, however, no doubt that there is an excessive or abnormal action of the thyroid. This is well seen in the clinical results achieved by surgery or X-rays

which bring about almost certainly practical disappearance of these states which otherwise would lead to the death of the patient as a rule for cardiac failure. Anyone, too, who has seen the records, such as those of Rowden—over 300 unpublished—of cases treated by X-rays, some of which have actually become myxœdematous as a result, cannot but be impressed with the relationship of the thyroid to the pathological states. The exophthalmos, however, when marked does not disappear although the patient has otherwise recovered. Incidentally such records show the efficacy of X-ray treatment *properly carried out.*

Whether the thyroid is the primary seat of the disease is another matter and many attempts have been made to associate it with disease elsewhere in the sympathetic or endocrine system. The failure to obtain evidence of increased thyroid secretion in the condition may be due to the fact that the secretion itself is abnormal. A large amount of evidence has accumulated which indicates an antagonism between the suprarenal cortex and the thyroid. Further than this it is not desirable to go, except as an interesting speculation. The possible withdrawal of the normal antagonists would be expected to result in over-action of the thyroid. It is now abundantly true that small doses of iodine may be of considerable benefit in hyperthyroidism. There is diminution in the basal metabolism, heart rate, together with a marked increase in body weight and a striking improvement in the general condition of the patient. (Frazer.) How this improvement is brought about it is difficult to see, and it is suggested by Frazer that there is an iodine deficiency relative to the needs of the body which the small doses of iodine can make up, although large doses make the patient obviously worse.

Apart from iodine treatment and surgery, all medical measures which tend to rest the patient physically and mentally are commonly recognized to be of great value. Not infrequently where it is possible, rest in bed is insisted upon prior to operation. It is found that the rate of the heart becomes noticeably reduced by such treatment. This is important, for the cardiac state adds greatly to the danger of operation. Also the active side of the sympathetic-parasympathetic system is thereby reduced, and that of the endocrine balances which are described in a later chapter. The cardiac condition found in hyperthyroidism has been dealt with in relation to the rate of the heart.

CHAPTER XXIV

BODY WEIGHT

Questions regarding body weight have to be answered daily by the practising physician. As a rule they fall into two categories:—anxious parents who consider their children are too thin, or are not growing rapidly enough; and middle-aged people who find themselves becoming too stout.

Body weight is indicative of the balance between energy intake and output. A brief consideration will here suffice to indicate the innumerable factors upon which it depends. There are great differences in various individuals, all of which we must consider as physiological and which depend on the stature. A man of five feet will be fat if he weighs 11 stones, but a man of the same weight and whose height is six feet will be thin. Stature depends largely on heredity, but how far this can be influenced by conditions of life and the internal secretions is a subject regarding which we have only a very general and vague conception.

In the chapter on "Growth" we shall see that there is every reason to believe that diet before the age of 25 may play a large part directly or indirectly through the ductless glands in determining stature. On the other hand, children reared in apparently similar conditions may vary appreciably.

When we consider the factors concerned we shall see that apart from stature there is little evidence that heredity plays much part in the determination of body weight.

Energy, Intake and Output.—Here it must be realized that energy intake is not synonymous with what goes in by the mouth, but is that part of the actual intake which is absorbed and made use of. Thus we find a baby which is fed each time it cries may consume enormous quantities of milk, yet it does not grow fat. Indeed it probably does not thrive at all. Actually a large proportion of the milk is found undigested in the stools, the so-called lienteric diarrhœa. The presence of this excess of material in the alimentary canal brings about irritation and pain, causing the child to cry and creates a vicious circle. In adults, too, the presence of undigested material in the stools will indicate faulty absorption. Excess of fat, for example, indicates that the fat portion of the diet is not being utilized and is usually a sign of pancreatic disease

and deficient secretion of lipose. It is commonly associated with pancreatic deficiency.

Not infrequently the actual intake is deficient as in starvation, in which case the individual utilizes first the carbohydrate stores of glycogen, then his fat, and later his protein. The starvation may occasionally be due to an inability to procure food. More often it is a matter of difficulty or pain on swallowing as is seen in œsophageal stricture, where, if gastrostomy is not performed, the individual starves to death, or in a case of gastric ulcer where the pain caused by the presence of food may bring about fear to eat. More commonly still the lack of intake is from lack of appetite which, after all, influences the intake and largely, as we have seen, the processes of digestion. Appetite is closely allied to hunger, but the two are not absolutely identical. Appetite may be considered to be almost a mental state and may occur in the individual who is not necessarily feeling the pangs of hunger. Hunger is the pain appreciated as the result of spasmodic contractions of the stomach and the sensation is somewhat similar to that of gastric ulcer, except that the situation of the latter is usually more towards the lower half of the stomach. Our knowledge of hunger we owe largely to the work of Carlson and his collaborators, especially Luckhart, who have subjected themselves to starvation. Hunger has been shown to be due to rhythmical contractions of the fundus of the stomach, and it has been found that the pains are in proportion to the contractions. These are superimposed upon the normal variations of tone of the fundus. As the stomach becomes empty, the contractions gain in intensity, and it is only when severe that they cause actual sensation. This is shown by passing a small balloon into the stomach and connecting it by means of a small tube to a tambour.

The effect of hunger depends greatly on habit. Some individuals can readily miss a meal, while in others this would bring them to the verge of collapse, as the result of an overwhelming feeling of weakness. It appears most likely that this is largely a psychical result of the sensations and from ignorance of the fact that the body has adequate stores of energy, since the eating of anything, even that which supplies no energy, will ameliorate the sensations. An Englishman visiting France feels positively starved by midday, but after a few days he becomes accustomed to a light French breakfast. Similar changes in hunger sensation can be noted in changing from a midday dinner to a light lunch and evening dinner. It would seem not improbable that hunger contractions are set up by a mechanism like conditioned reflexes. We know, for example, that if a bell is rung half an hour before a dog is fed, the dog will

eventually salivate regularly at the end of the half hour, although no food is produced. We can readily imagine that the stomach contractions occur when the stomach is empty and when the habitual time for filling arrives. The hunger movements have been shown to begin before the stomach is absolutely empty, and possibly the onset depends on the habitual amount of filling, for an individual accustomed to large meals feels hungry just as rapidly as one who eats little, and this fact bears no relation to their energy output. If the hunger pain is not treated after a few days it weakens and there may be an actual disgust of food. So "hunger striking" is not so difficult once the first few days and the enthusiasm are past. It is indeed interesting to note that Carlson remarks on the great sense of well-being and vigour which succeeds such a fast.

The above is of considerable clinical importance as it indicates that the incentive to eat is largely habit. Over-eating and under-eating tend to be continued to the detriment of the individuals concerned and it is only by inflicting considerable hardship during the preliminary few days that the habits can be altered. We see, too, the great disadvantage of the taking of snacks and the eating of sweets between meals, as these, like anything else, mitigate the sensations of hunger and reduce the appetite, and habit of reduced appetite is readily established. Under-eating is common in neurasthenic women who tend to become thin and suffer from neuritis, which appears to be commonly associated with deficient fat in the body, and the extent to which such individuals benefit from temporary hydro-life and the incentive to eat is notorious.

In a large number of individuals excess of energy intake is a habit almost to the extent of a disease. Such persons have apparently so stretched their gastric mucous membranes that they do not feel replete until they have consumed an amazing amount of food. They apply to the physician for advice and are disgruntled when they are told the truth.

In the Treatment of Obesity or excessive storage of energy there are three possible methods, diminution in intake, increase in output of external work, or increase of the internal work or basal metabolism. The first and second are to be advised for preference but may be extremely difficult to obtain, while the third requires a minimum of effort on the part of the individual. It must, however, be realized that no advantage is gained if the hunger brought about by increased work is satisfied by increased intake. All the factors must be considered. Further, the real meaning of reduction of intake is seldom appreciated by the layman. Only too often, if sugar and potatoes are cut off by the physician, an additional supply of bread is taken. Only recently there came to the personal notice of the writer the instance of a lady of 15 stone who had

been forbidden carbohydrates and had a list of articles of diet to be excluded. She consumed, however, over half a bottle of port a day as she felt the lack of food so much.

In relation to exercise, too, it is well known that some stout individuals walk a great deal. This will be dealt with when the effect of exercise is considered, but suffice it here to say that an adaptation occurs to habitual exercise of moderate degree and less fuel is used. Therefore the exercise recommended for weight reduction should be that to which the individual is not accustomed for preference unless the exercise is unusually severe. Lack of physical exercise is a very common cause of obesity, and a vicious circle often becomes established, as the lack of exercise causes obesity, and obesity makes the individual disinclined to take exercise and liable to fatigue even if it is moderate. Fatty heart readily ensues with all the signs and symptoms of cardiac insufficiency. If the diet is only slightly reduced, so that it is just not positively uncomfortable, then it will take a long time to cause any noticeable loss of weight. The *régime* will have to be persisted in for many months. Much of the so-called inherited tendency to obesity is more often acquired, being due to appetite and sloth, though the victims would stoutly deny such suggestion. It must also be recognized that over-eating may be a thing of the past, and energy intake may now almost balance output. Any energy stored as fat will not disappear until it is actually required for use. In practice the best method is to get the patient to demonstrate to himself or herself the effect of diet on body weight, and to set a standard of loss to be attempted every week.

Increase in basal metabolism offers the laziest way of getting thin. It may be brought about by excessive protein eating, which at the same time gives satisfaction as to the amount consumed. Care must be taken that the meat is really lean. As a temporary measure thyroid administration may be undertaken. So long as the pulse is under 100 per minute, this treatment may be considered safe. In general there is much to be said against this practice (see page 204). In any case it is so dangerous that it cannot be left in the hands of the patient without proper supervision. The dose must be in terms of the dried extract, since, as pointed out by Dixon, many commercial preparations contain only one-fifth of their weight as such. A small proportion of stout people suffer from want of balance of the internal secretions, but even in these hormone therapy is secondary to dietetic measures and increased energy output.

In the young, body weight and growth are almost inseparable and it is customary to consider the weight as an indication of whether or not a child is thriving. Unfortunately it is imagined that the growth depends entirely on

what the child can be persuaded to consume and many better-class children are overfed often with patent foods. In the poorer classes one meets with underfed babies and more commonly badly fed babies. Barley-water and all sorts of uneconomical preparations are used intentionally as substitutes for milk, and some mothers have apparently no conception of what a child can digest. Only recently the writer when in a shop inquired as to the cause of the severe distress of a baby in an adjacent room. The explanation was that the grandmother was endeavouring to "shove some treacle pudding into it" as it wasn't thriving. When it is considered that the child was but a few months old the necessity for baby welfare clinics is well seen.

The physiological principles in the feeding of infants and its regulation by regular weighing are really quite simple and clear. A normal child when born weighs from six to eleven pounds, and in the first week a few ounces are lost, no doubt as some of the stored energy is utilized in activity, and as lactose is not fully established. Thereafter there is a gain in weight from 3 to 6 ounces per week, which is continuous, except for the time of teething, when there may be an interruption. During the first nine months the ideal food for the infant is its mother's milk, provided the mother's diet is adequate in respect to growth factors (see "Vitamins," page 197). The importance of ante-natal care, as well as post-natal, in this respect is now being realized. It is a significant fact that all wild animals bear their young in spring and early summer, when not only is additional heat available, but vitamins are most readily available. The best substitute for human milk is cow's milk, provided the cows are properly fed, and here it may be mentioned that cabbages, kale, and turnips are a convenient source of vitamins for animals fed indoors in winter.

The milk should also be from cows which have passed the test of tuberculosis, but to the disgrace of our modern civilization be it said that this appears to be economically impossible at present. The provision of special dairies for the provision of nursery milk is a very necessary institution in all cities. Sterilization, it is true, is a safeguard against tubercle, but even pasteurization destroys the growth factors in the milk and these therefore have to be otherwise supplied.

Artificial foods are of value in proportion as they approximate to the natural milk, but nothing is to be gained by excessive feeding of an infant. Fat babies do not necessarily become any the better adults and not infrequently the attempt to make them so results in serious upset of the alimentary tract of the infant. The following gives sufficient energy intake for any child:

Six feeds a day consisting of 20 minutes at the breast, or 3 to 7 ounces of milk from a bottle according to age is *ample* for any child in the first nine months. As the chemical constitution of cow's milk differs from human milk, to the former must be added 1 ounce of water in each feed to dilute the fat, together with 1 teaspoonful of sugar (Demerara sugar is a convenient laxative) to make up the sugar content. Some physicians further add 2 grains of sodium citrate to each feed to prevent the formation of large milk clots.

The intake of an individual may be adequate, digestion and absorption efficient, but the absorbed food not properly utilized. This is well seen in diabetes, where the carbohydrate is absorbed but is not sufficiently rapidly burnt, so that it accumulates in the blood and escapes in the urine. This is, however, but an example of the influence of the internal secretions on metabolism.

The Relationship of the Endocrine Organs.—Our knowledge regarding the relation of these organs to body weight is as yet somewhat obscure, but that there is some relation is now reasonably well established by clinical and experimental observations. There is not the slightest doubt that many cases of gross obesity are definitely related to deficiency in the ductless glands especially the pituitary body. As, however, there is no general acceptance of any definite view, the subject is dealt with in a special chapter on "The Endocrine Balance."

CHAPTER XXV

GROWTH

The clinical phenomenon of growth depends on the power of the cells which make up the body tissues to multiply. Each variety of cell has its own conditions of growth, but each is integrated to form the normal body structure. For the growth of the body as a whole many factors are concerned. The most important is undoubtedly that of diet.

Diet.—The essential principle of diet in relation to growth is that there must be supplied not only fuel for energy and substances necessary to make good the normal wear and tear of the body as in the adult, but sufficient for the building up of new cells. Certain tissues, such as bone, may require an increased intake of certain substances (calcium and phosphorus), apparently in excess of what is necessary for adult life. The possibility of the interference with metabolism of such substances has received considerable attention in the past few years, but until we know accurately the exact mechanisms of their metabolism and the exact rôle which they play in the growth of the tissues, it is not to be expected that we can do anything but guess how pathological conditions are produced. Fortunately Nature as a rule provides such salts in abundance at the time when they are necessary. It will be obvious that a child whose diet is deficient cannot be expected to grow and the general ignorance in such matters is truly appalling. It is no uncommon thing for a parent to imagine that rice or barley water may be substituted for milk, although, if the child has been overfed with milk, such reduction of its diet may be of advantage provided it is not kept up too long. Similarly also it is difficult to eradicate the giving of lime water with a view to increasing the calcium intake when in reality less is contained in this fluid than in milk.

In general the body weight may be taken as an indication of growth, although this cannot be said unreservedly. If, for example, a child is fed on excess of carbohydrates, so common in patent foods, a large amount of energy is supplied, the excess of which may be stored as fat. But the child does not grow if the food has not an adequate biological value (see page 186), that is, supplies the other factors, other than energy, necessary for growth. In the latter respect milk and meat take first place, no doubt because of the number of

amino-acids they contain which are suitable for the building up of human proteins. In the adult we have seen that the biological value of the diet is not so important, as adults appear to have the power of synthesizing certain of the essential amino-acids which a child has not.

Should the metabolism of the infant be excessive in its having to counteract some infection, such as syphilis, tuberculosis, or various intoxications, it will, of course, tend to interfere with growth, as unnecessary energy is used up.

Vitamins.—The diet must also contain an adequate supply of the accessory food factors, and, indeed, it was failure of the young animals to grow on a diet deficient in these substances which led to the discovery of these bodies. No method of reducing this factor is more efficient than complete sterilization of the food in an attempt to protect the child. For purposes of convenience these so-called vitamins have already been discussed in Chapter XXII, in which also the importance of *light* is pointed out.

The above presumes that the child possesses no abnormality which prevents the intake of food. Mechanical difficulties in sucking or pain caused, say, by stomatitis are common causes of diminished intake. The mere giving of food, also, in abundance may be of no value if the powers of absorption from the intestine are deficient. Various forms of enteritis interfere with absorption and no factor is more potent in the production of such conditions than a faulty diet, especially, according to Hutchinson, excessive fat.

Certain of the endocrine organs also play an important part in growth and have to be considered in this connection.

Thyroid Gland.—Forty years ago it was noted by Kocher in Switzerland that patients from whom the complete thyroid had been removed bore many resemblances to *cretinism* which was so common in that country and he noticed further that in this latter condition it was very difficult to palpate the thyroid. The relationship of the gland to such conditions was clearly shown by Schiff in 1884, but it is only in comparatively recent times that the rôle of the thyroid in relation to growth has been clearly understood. The thyroid we now know is responsible for the elaboration of a substance which is a stimulus of general metabolism. In the adult this serves to give a greater range of metabolism and consequently a greater sphere of activity. The disadvantages of strict limitation in this respect are seen clearly in myxœdema and exophthalmic goitre. In the child the hormone produced is responsible not only for the general metabolism, but also for the general growth of tissue, or, put differently, for the speed of metabolic and proliferative changes in the individual cells. This fact was first

shown clearly by Gudersnatsch, who found that the speed with which tadpoles metamorphose was greatly increased by the administration of thyroid extracts.

Clinically, the effect of deficiency of thyroid on growth is seen in the condition of cretinism in which the child remains infantile and all its functions and tissues are retarded. Similarly all organs whose functions are dependent on the metabolic rate are affected (see page 190). The growth of the skeleton is slow and ossification is delayed, while the cold dry skin covers a myxœdematous integument, giving the child a short thickset appearance and bloated countenance. According to John Thompson these features are seldom marked at birth with the exception of a swollen protruding tongue, a fact which suggests that prior to birth the thyroid of the mother supplies the necessary hormone. The fact, however, that since the introduction into general use of thyroid extract in myxœdema there has been a diminution in cretinism, even in those areas where it used to be very common and in which myxœdema is still common, gives weight to the statement that the mother of a cretin must also to some small extent suffer from hypothyroidism. More commonly the mental dullness which results from impairment of cerebral growth first attracts attention and this, together with the stunted figure and the delayed closure of the fontanelles, is sufficient for the diagnosis which is confirmed by the marvellous effects of thyroid administration. The conversion of a potentially idiotic dwarf into a useful member of society by the administration of the extract is one of the triumphs of modern science and is a striking example of how the surgeon and physician and pathologist have contributed to physiological science and how the co-operation of all has been of benefit to mankind.

The Pituitary Body.—The anterior lobe of the pituitary body exercises a special function in relation to the growth of bone. Over-activity of the gland in a young person before the epiphyses have joined leads to a general overgrowth of the skeleton and to the production of gigantism. In adults, however, when the long bones have attained their maximum length, similar activity results in *acromegaly* in which only certain areas are affected. The hands and feet enlarge greatly in size and become characteristically spade-like, while the growth of the bones of the face effects a profound transformation in the countenance of the individual, which is characterized by heavy plainness. Final confirmation of the condition is obtained by an X-ray photograph of the skull which reveals that the sella turcica has become enlarged to accommodate the gland. At the same time general metabolic changes occur from at first stimulation and later destruction of the posterior part of the gland which is more intimately related to metabolism especially that of carbohydrates.

Underactivity of the gland results in dwarfism from undergrowth of the skeleton which is commonly associated with a great tendency to adiposity and since this is particularly prominent in the region of the genitals the condition is designated *adiposis dolorosa genitalis*. The tendency to the deposition of fat in such cases will be dealt with in relation to "The Endocrine Organs."

Racial and other hereditary characteristics undoubtedly play a considerable part in the determination of stature and no doubt obey the ordinary laws of inborn characteristics. How far these characteristics are determined by hereditary variation in endocrine activity is extremely difficult to say, but the fact is that poor hygienic conditions and faulty diet, such as occur amongst the dwellers of slum areas, lead undoubtedly to impairment of mental and bodily growth. It is possible that they may bring about their effects by affecting the endocrine system and indeed recent evidence suggests that vitamin deficiency so common in such conditions may affect growth in this way. More than this it is most dangerous to postulate.

Whether the above are all the factors on which growth depends we do not know. Unfortunately clinically we still find cases of so-called primary wasting or marasmus which have no obvious cause and which only too frequently have a fatal end. Fortunately these cases are becoming fewer because they are dealt with at an earlier stage than heretofore and so toxic and like conditions are treated. Undoubtedly many children who would otherwise have become marasmic become quite normal when placed in physiological surroundings and on a physiological diet. Many diseases affecting chiefly the bones are as yet not understood, such as achondroplasia, Paget's Disease, and osteomalacia. Why, however, in certain conditions the bones of some regions are affected more than others remains unexplained. Thus in chronic pulmonary conditions, clubbing of the fingers is sometimes observed due to definite enlargement of the terminal phalanges and more rarely of the ends of the long bones, while the face escapes. On the other hand, in that rare condition, known as leontiasis ossea, the skull bones are the seat of a peculiar overgrowth.

Local Growth.—The mechanism of the control of local growth is not only one of the most interesting problems of physiology, but one of the utmost clinical importance as pathologically local overgrowth of tissue not infrequently takes place. Such an overgrowth may be confined to certain tissues and remain circumscribed, such as skin epithelium in the simple wart, while on the other hand a certain tissue may invade other tissue; we have again an example in skin epithelium, producing an epithelioma, a form of cancer. Unfortunately in such conditions, we are quite in the dark as to why one tissue should break

its boundaries, except that in many instances irritation, and in some instances a specific virus, is to a large extent responsible for local overgrowth. Within recent years, however, it has been found possible to grow various tissues outside the body in suitable media and other sterile conditions after the manner utilized for the culture of organisms in bacteriology. For adequate growth the cells have to be supplied with suitable nourishment, but what is of still more interest is the fact that the speed and nature of their multiplication may be influenced by other tissue cells and their extracts. Normally each tissue adheres to a certain boundary concordant with normal function, although how this balance is maintained we do not yet know. This problem is a very essential one in the study of neoplasms in which an excessive proliferation of certain cells occurs, with, in the case of malignancy, the power of invading other tissues. A great advance in this field of work is anticipated in the near future as the result of the developments in tissue culture, and the discovery of specific substances (Gye) which bring about abnormal proliferation and invasion.

Normally the great stimulant to local growth of tissue is use. The efficiency of every organ in the body is benefited by use, and where it is necessary to obtain increased efficiency, an actual tissue hypertrophy may be brought about. Thus, there is an increase of muscle tissue for heavy muscular work or an increase in kidney tissue with excessive drinking. How the work stimulates the increase is unknown, but it appears that whenever an amount of work is such that there is no reserve in the tissue, an increase results so as to create a reserve and make it possible for certain areas to rest intermittently (see page 293). How far this principle can be carried is uncertain, but it does play a part. We are familiar with the thickening of the skin of the hand which occurs in manual labour, and indeed if this is begun at an early age the size of the hands often becomes increased. Many observers have endeavoured to apply the principles to disease. Arbuthnot Lane, for example, has emphasized the relationship between occupation and arthritis deformans in which there is an overgrowth of the bony structure of joints and in which, for example, the knee of the miner or the hands of the pianist are commonly affected. Or, again, according to the same principle, it is possible that excessive utilization of the vaso-motor system from excessive physical or mental work or various intoxications may lead to an arterial overgrowth which, like all other overgrowths, is abnormally liable to degeneration. The utilization factor is often extremely difficult to evaluate and determine as undoubtedly other factors are concerned. Otherwise all individuals having the same occupation and living under similar conditions should be similarly affected, although it is true that

often circumstances of life of different individuals appear more similar than they really are. In these, like so many other conditions, physiological, pathological and clinical investigation must go hand in hand and such active co-operation must always be more fruitful in that it gives a more complete view than a policy of each independently waiting on the advance of the other.

CHAPTER XXVI

SWALLOWING. DIGESTION

SWALLOWING

Swallowing is of more interest to the physician than at first sight would appear. Not only does physiology throw a light on certain states of dysphagia found in disease, but these states also throw considerable light on the physiology. In swallowing, three distinct mechanisms are involved. First the food is pushed by the musculature of the mouth into the pharynx. Here it sets up a reflex by which the complicated movement of the pharyngeal muscles is brought about while the superior sphincter of the œsophagus is opened. That the œsophagus is normally kept shut does not appear to be well recognized, although it obviously must be so, otherwise air would get sucked into it, since, as has been pointed out by Negus, the upper end of the œsophagus is normally closed by the sphincter assisted by the rotation of the cartilages of Santorini. These two phases result from the action of striated voluntary muscle, while the third, by which the food is carried down the œsophagus to the stomach, depends on the involuntary muscle of the gullet. Clinically we may see all three phases upset. Upset in the first phase is fortunately rare, but may be seen in bulbar paralysis, which also affects the second stage. Simple interference with the latter, however, is best seen after nose operations when cocaine from the nasal packing has anæsthetized the mucous membrane of the pharynx. The food is forced into the pharynx, but the reflex mechanisms of the latter and the opening of the œsophagus does not take place and nothing further happens. Besides being intensely disagreeable and alarming to the uninitiated, in young children it might be clearly very serious.

Dysphagia may obviously result from pathological conditions obstructing the œsophagus, from within or without, such as a neoplasm, an aneurysm, or any condition where there is an inflammatory lesion in the vicinity of the food passages, e.g. larynx, pericardium or œsophagus itself. The proper sequence of events in the act of swallowing can be shown experimentally to depend on the nervous and not on the muscular connections. This is also seen clinically in cerebellar conditions, such as thrombosis of the inferior cerebellar artery, in

which condition the lack of co-ordination in the muscles of swallowing is well seen and may be the most frightening symptom. Of clinical interest, too, is the reflex by which stimulation of the pharynx brings about a relaxation of the cardiac sphincter.

Spasm of the sphincter or its failure to open is a common phenomenon and cardio-spasm may result. A simple form may be seen from eating very dry food, say sandwiches in the railway train. The food is swallowed, but from lack of lubrication passes down the œsophagus so slowly that by the time the lower end is reached the cardiac sphincter has closed again, and the effort of the œsophagus to drive the bolus into the stomach may be extremely painful. Such spasm is not infrequently seen in hypochondriasis or hysteria, and from its reflex nature obviously the longer it persists the more difficult it will be to get rid of. So far as the author knows such spasm has never been associated clinically with any special anæsthesia of the pharynx, but from the physiological point of view this seems quite probable and we know that in the hysterias diverse anæsthesias are common. Cardio-spasm, although in the first instance of purely functional origin, may, however, if it persists, lead to definite pathological dilatation of the œsophagus.

DIGESTION

In its complete physiological sense digestion refers to all the processes by which food is prepared for absorption. These processes begin at the mouth and are continued to the ileo-cæcal valve. The actual chemical processes of digestion and metabolism are discussed elsewhere (see Appendix A). While, unfortunately, we know little of the physiological mechanisms regulating the secretion of the digestive juices of the small intestine, other than that of the pancreas and bile, we are fortunate in having, at least so far as we know, few clinical conditions in which these mechanisms are upset. Digestion, as we meet it clinically, refers to gastric digestion and the term indigestion refers to pain in the region of the stomach. The factors upon which complete gastric function depends are very complex, not only in themselves, but also as they are influenced by the condition of the bowel further down, especially by stasis. The stomach serves as a container, while it also continues, for a time, carbohydrate digestion, and initiates protein digestion. It is also of importance in sterilizing and warming the food. Further, to carry out its function adequately it must also pass on its contents at a reasonable speed.

Mastication.—The preliminary process of grinding is undoubtedly of first importance, for food inefficiently broken up tends to be held up at the pylorus.

Further, in chewing, the flavour of the food is appreciated, without which the secretion of digestive enzymes is reduced, while the presence of food in the mouth facilitates the digestion of carbohydrate by salivary digestion.

Salivary Digestion.—This depends for its efficiency on (1) the admixture of the substances to be digested, e.g. the starches, with the saliva, (2) the amount of salivary diastase or ptyalin secreted, and (3) the time it is allowed to act.

The first factor concerned is, as indicated above, satisfactory mastication. The amount of saliva secreted varies in the first instance with the relish with which the food is anticipated and taken, and here, as in the secretion of gastric juice, psychical impressions play a most important part. Also it can be shown that these impressions form a true reflex of what we know as a conditioned reflex with an afferent path from the sensory organ such as the eye, taste buds or nose, and an efferent path to the effector organs, the salivary glands. Once this reflex is established in association with definite conditions, it continues in the presence of these conditions whether the original sensory organs are stimulated or not. For example, a dog always fed to the accompaniment of a certain note of the piano will secrete saliva reflexly when this note is struck although the food is not actually produced.

Salivary digestion is under the control of two sets of nerves, the sympathetic and the parasympathetic, e.g. chorda tympani. The latter is responsible for making the saliva more fluid and the former for making it thicker and more mucous. In the past several dogmatic assertions were made regarding the nature of these secretions, but animal experiment on this point has given such varied results that further work is now necessary. It is, however, known that the secretion produced varies appreciably with the nature of the stimulus. Thus dry food causes greater secretion than moist food, and it is held by some that the more carbohydrate there is in food, the more ptyalin is secreted.

The effect of the higher centres on salivary secretion is a matter of everyday experience. It is inhibited by emotion, such as fear. The old trial by ordeal in which the suspect had to eat a quantity of dry flour depended for its efficiency on this physiological fact. In the same way the thirst of public speakers can be accounted for. Of great clinical importance is the extreme thirst after atropine administration, which causes paralysis of the nerve ends of the parasympathetic. A similar condition occurs in facial paralysis, in which the salivary fibres have become involved and disturbances of salivary secretion are met with in disease of the central nervous system affecting the salivary innervation.

It used to be taught that ptyalin was active only in alkaline solution, but it has now been shown that it is even more active in neutral and faintly acid solution. The drinking of acid wines is not then of such importance as was imagined. The fact that ptyalin digestion can continue in faintly acid solution must be of great value in the continuance of salivary digestion in the stomach.

We shall see later that the movement and distribution of the food in the stomach are so arranged that the entering food passes into the centre of the food already there, and that until the food passes the pyloric end of the organ there is little mixing of the food provided it is not too liquid. This procedure prevents the food from coming into contact with the hydrochloric acid secreted by the gastric mucous membrane, and thus the inhibition of the ptyalin is delayed.

That the digestion of starch actually does continue in the stomach in man may readily be seen by the fact that when the evacuation of the stomach is delayed experimentally or as a result of severe exertion, it is found that a considerable amount of starch is digested. (Campbell, Pembrey, and others.)

Protein Digestion in the Stomach.—The efficiency of protein digestion depends on the admixture of the protein with the digestive juice and the adequate secretion of the latter.

The admixture of the protein with the gastric juice depends in the first instance on how fine the protein particles are or how easily they can be separated. This again depends on the physical nature of the protein and the efficiency of mastication. On the physical nature of protein depends the reputation of the special digestibility of white meat, such as chicken and fish, which are not only easily masticated, but the digestive juice can penetrate more readily between their fibres than between those of red meat. In the same way white meats have less fat than red, a point of importance, as fat not only prevents the access of the pepsin and hydrochloric acid to the protein, but actually tends to inhibit the secretion of gastric juice and cause delay in emptying. Certain fishes, such as mackerel and salmon, have for similar reasons a reputation for indigestibility. These matters are only worthy of serious consideration in individuals whose digestion for some reason or other has become impaired.

The amount of gastric juice secreted depends on two factors, the relish with which the food is taken, and the nature of the food itself.

The original observation of Pavlov on dogs indicated the importance of the anticipation of food or *psychic secretion,* but from recent work, especially that of Carlson, on a patient with an œsophageal obstruction and a gastric fistula, it does not appear that this psychic secretion is so important in man as was

first thought. No doubt individuals may vary in this respect and may further vary according to the actual state of hunger or otherwise they happen to be in at the time of the experiment. We also have seen above that it is common experience that the psychic secretion does influence salivation in man. The passage of an alkaline secretion such as saliva into the stomach will, we know, stimulate the gastric secretion of HCl and we may consider that in this way the higher centres have indirectly an influence on gastric secretion.

The actual *satisfying of the appetite,* both in man and animals, has been shown to be particularly important even although the food does not reach the stomach. A reflex is set up by the stimulation of the olfactory and gustatory nerves, and obviously varies with the palatability of the food. We know (from the work of Hornburg, in 1904, who investigated the case of a boy with gastric fistula) that it is not the mechanical act of chewing which is responsible for the increased secretion. The chewing of an indifferent substance such as india-rubber did not cause secretion, while other tasty articles of diet, as was also shown in the case of Carlson's, caused marked secretion. In Carlson's patient, for example, the more he liked certain articles of diet, the greater was the rate of secretion of gastric juice. This reflex comes under the classification of conditioned reflexes and depends on the previous association of some particular taste and smell in the past. This has been further dealt with on page 41, where this type of reflex is discussed more fully.

The importance of studying the likes and dislikes of a patient from what has been said above cannot be over-estimated, especially in patients recovering from illness in whom the digestive secretions are often reduced. This aspect is of importance in the training of the young.

The giving of highly flavoured foods to children is in this respect pernicious, as it tends to cause the more staple articles of diet to appear uninteresting and tasteless and subsequently difficult to digest. It is, however, interesting to note that many of the dislikes of children are brought about by monotony, especially of a carbohydrate diet, and we know that a dietary over-balanced in this respect has certain disadvantages. From the point of view of vitamins it may be said that seldom are dislikes formed for the more natural foods, although this does occasionally occur.

The chemical nature of the food also plays a considerable part in causing the secretion of gastric juice, and it is due to this that secretion continues after food has been taken. Several articles of diet have a directly stimulating effect on gastric secretion. The better known are the extractions of meat. Indeed, this is practically the only value of substances such as beef tea and

bovril which have little or no food value, unless special measures are taken in the making of them up. It has also been shown that drinking water has a markedly stimulating effect on secretion. Drinking at meals is disadvantageous from the point of view of salivary digestion as it is a diluent, but clearly it may be beneficial as far as gastric secretion is concerned. The best time to drink is immediately before a meal, when the water has time not only to stimulate secretion but at the same time to wash out the stomach.

Of special interest is the effect of the *products of digestion,* particularly peptone and dextrin. It was found by Elkins that if such substances are boiled with cells from the pyloric end of the stomach and the decoction neutralized, filtered and injected into a vein, gastric secretion is stimulated. We may take it, therefore, that normally when such substances come in contact with the pyloric end of the stomach, a substance to which the name of "gastrin" has been given is produced which, when absorbed, causes the stomach to secrete. More recently it has been demonstrated by several workers that histamine (a putrefactive derivative of protein) has a similar effect, and in the light of this the existence of gastrin appears to require further investigation. No doubt it is to the increased secretion which results from the absorption of the putrefactive substances that the practice of hanging certain game, such as grouse, to improve its digestibility owes its value. The tissues also become softened.

Some substances, on the other hand, have little or no effect, or may even inhibit the secretion of gastric juice. In this latter respect fats are especially powerful, a point of considerable therapeutic importance, as we shall see below. This fact also suggests that in the ordinary eating of meat the fat normally counteracts excessive stimulation by the extractives and products of the protein metabolism. Substances, such as white of egg, bread and starch, are among those which have no effect on gastric secretion.

If the foregoing indicates anything, it shows how well mankind has established his habits in accordance with his physiological mechanisms. The fact that individuals of a household usually have their meals at the same time, besides being a convenience, tends to make the repast more light-hearted and to discourage pessimism and anxieties. In this way and by the general appurtenances of the table everything is done to encourage the psychical effects and the relish with which food is taken. Individuals who take their food alone, which usually means also hurriedly, are notoriously apt to be subjects of gastric disorder.

Tasty *hors d'œuvres* and soup act as stimulants for the digestion of the more solid protein courses to follow. Sweets as carbohydrates are added later and

at a time when conditions are most suitable for the continuance of salivary digestion on the stomach. Fruit subsequently cleanses the teeth. The addition of potato to the protein does not have any good basis, but on the other hand the addition of cream or butter to carbohydrates will by reducing acid secretion assist salivary digestion.

The beneficial effects of alcohol at mealtime can be attributed to the fact that it tends to lessen the sense of fatigue and increase the sense of well-being with the result that the food is taken with more relish. Some assert that the main action of bitters, which have a considerable reputation as stimulants of digestion, is through the alcohol in which they are commonly taken. Recent accurate work by different workers on the gastric contents of man has certainly failed to show that gastric secretion is increased by bitters, but it appears uncertain that the absorption necessary for the action of bitters had taken place, a point insisted upon by the older exponents of Materia Medica. Although the modern sciences of physiology and pharmacology are as yet uncertain as to the method of their action, there is so much clinical evidence of their therapeutic value in gastric conditions that they cannot be ignored, and their action may be yet satisfactorily explained.

The influence of the palatability of the food indicates the importance of cooking which Macleod aptly refers to as the only digestive process over which we have direct control. In this respect we prefer the many-course dinner to the large amounts of one dish, but this is really a matter of habit, as one dish which may be appetizing to one individual may be revolting to another, e.g. oysters. There are many accustomed to so-called plain fare, which usually means indifferently cooked fare also, who appear to thrive on it. Of these it can simply be said that it is well that they have not often tasted of better things.

Control of the Acidity of the Gastric Contents.—The acidity of the gastric contents has for many years been appreciated, and its clinical investigation has frequently been of value in diagnosis. The factors which may influence it are therefore worthy of attention. We have seen that the gastric secretion is initiated reflexly, and is continued as a result of a chemical process. As secreted it contains about 0.4 to 0.5 per cent. of hydrochloric acid. After admixture with the food and partial neutralization, the percentage falls to about 0.2, which is almost at the optimum of hydrogen ion concentration for the action of pepsin. As the neutralizing elements become used up there is a tendency for the acid in the stomach to rise. This it does slowly until about two and a half hours after a meal when there is a drop in the free hydrochloric acid content. This has now been shown to be due to the neutralization of the acid, due to

regurgitation of the alkaline contents of the duodenum through the pylorus. There is, in other words, a normal mechanism (until comparatively recently unrecognized) by which the amount of free acid in the stomach is not normally allowed to exceed 0.2 per cent. A maximum is reached about one and a half hours after a meal, and thereafter falls, until in the resting period the total acidity is only about 0.03 per cent. This contribution to physiological knowledge, founded on the work of Boldryeff, we owe mostly to clinicians, especially to Bolton.

It is supported by the results of operations, although curiously enough it was not with this in view that the operations were originally carried out.

It seems quite likely that the opening of the pylorus for the purpose of regurgitation may be under chemical control. The early findings of Pavlov, later elaborated by Cannon, to the effect that the pylorus was controlled by conditions of alkali or acid on each side of it, and which Cannon considered to indicate the normal mechanism of evacuation of the stomach, may really refer to the normal mechanism of regurgitation. With the recognition of pyloric regurgitation as a normal mechanism appears the explanation of the common "bilious attack." It seems that some quality of the food, commonly excessive fat * or sugar, which may cause a late hypersecretion, causes an exaggeration of the regurgitant mechanism instead of the normal evacuation. As a result, bile is brought into the stomach and gives the character to the typical bilious vomit. This explanation is supported by the fact that there is usually retention, even an increase, of gastric contents, and a disagreeable sensation relieved by vomiting. The bilious back-flow may continue to some extent for several hours.

In investigating gastric contents the two methods commonly in use are those of Ewald and of Refuss. In the former a test meal is given consisting of a pint of tea and a small piece of toast at breakfast time, and after an hour the stomach contents are siphoned off with a stomach tube. In the latter method the patient swallows an Einhorn tube which he can retain in position for long periods and through which samples may be drawn off by syringe every quarter of an hour. This tube is of rubber and of small bore, so that it can be swallowed and retained in position with little discomfort. In this instance the meal contains a pint of oatmeal porridge made from two tablespoonfuls of fine oatmeal and strained through muslin to facilitate aspiration.

In carrying out a scientific investigation of gastric contents the Refuss method certainly gives the most complete information, but it is clear that to be

* In the case of fat we know such late hypersecretion and retention does occur, although in the first hour secretion is reduced.

really complete an estimation of the chlorides, which is commonly omitted, is as important as investigation of the hydrochloric acid in virtue of the now recognized neutralization by means of duodenal regurgitation. Otherwise it is impossible to differentiate between cessation of secretion and neutralization, which will be indicated by no decrease in the level of the chloride content, although the hydrochloric acid content may diminish. As time, however, is often of importance such investigation cannot always be made and clinical laboratory workers claim to obtain a large amount of information from estimations of the hydrochloric acid and free acidity only. An excessive amount of free hydrochloric acid after an hour used to be considered an indication of hyper-secretion, but now we know it is more likely to be due to pyloric obstruction from organic change or functional spasm. By the Refuss method this is made still clearer by the failure of the hydrochloric acid concentration to fall. A true hyper-secretion shows itself not only in a large increase in hydrochloric acid, but also in the chloride. But recent work has shown that this condition is really quite rare.

If the stomach be emptied before the Ewald meal to avoid errors of dilution and incidentally to obtain evidence of undue retention, a considerable amount of information can be obtained by this method. Its comparative simplicity has much to commend it, while its value is enhanced if the chlorides also are estimated.

Movements of the Stomach.—A knowledge of gastric movements is becoming more and more essential for an understanding of gastric symptomatology, for, with the exception of the coarser sensations of heat and cold, all sensations are associated with contraction of the gastric musculature. It has been suggested that pain is caused by anæmia of the nerve endings. In this way it is similar to the cramp in skeletal muscle. This seems quite reasonable, and the severe pain of that rare condition—embolism of the mesenteric arteries—would similarly be accounted for. All gastric pain can be looked upon as being of muscular origin.

Functionally the stomach is divided into two parts, in a way reminiscent of the actual anatomical division of the stomach in ruminants. The proximal end is composed anatomically of the fundus and half the body and this forms the gastric reservoir where the food is stored under a small amount of pressure. The stomach wall simply adapts itself to its contents whatever the amount and exerts a postural tonus similar to that of the bladder. At the cardiac opening the sphincter and its immediate neighbourhood are normally kept contracted, but, as we have seen, are relaxed reflexly on stimulation of the pharynx by

food. On relaxation, not only is food allowed to enter the stomach, but by relaxation in its neighbourhood, room is made for more food, which then in virtue of the anatomical position of the cardiac opening passes into the centre of the food mass in the stomach. This has been substantiated by much recent work since it was first recorded by Grützner. In this way salivary digestion is allowed to continue in the stomach for some time, that is until the ptyalin is inhibited in the centre by the penetration of the HCl and provided the food is not too fluid. It is well to remember, too, that ptyalin is most active in neutral or in very faintly acid solution and not only in alkaline solution, as used to be imagined.

The distal half of the stomach one may call the gastric churn, as in it the food is churned up with the pepsin and hydrochloric acid and rendered sufficiently fluid to pass through the stomach. Anatomically we may say that the two halves of the stomach are divided at the middle of the body (incisura angularis), a region of considerable functional importance, as the work of Cannon and others has amply demonstrated. From this point the peristaltic waves sweep towards the pylorus and churn up the food. From experiments on animals Cannon rather emphasized the fact that the waves begin at the incisura, but there can be no doubt that in man some waves are seen in the fundus. These waves carry the food forward slowly, but as they travel faster than the food itself they override it and in so doing churn up the contents; hence the food is gradually wafted towards the pylorus. The existence of these waves can readily be demonstrated by means of X-ray observation and when the abdomen is thin they may be seen through the abdominal wall in cases of obstruction of the pylorus in which they are exaggerated. All modern evidence seems to show that the waves are continued past the pylorus into the duodenum provided there is no condition in the stomach which causes spasm of the pyloric sphincter, such as ulcer, insoluble lumps of food, excessive acid or conditions which cause spasm. This latter fact is the only part of the older view of Cannon which has been retained, as there is now no doubt that alkaline and neutral fluids leave the stomach without undue delay. It is to be noted that the goal of the waves is the pylorus, a point of importance in determining where any artificial exit should be made from the stomach and if the pylorus is patent, food will in virtue of the muscular arrangements tend to pass through it, although there is an exit elsewhere. Cannon has pointed out that different foods are retained for varying times in the stomach; for example, carbohydrates, if taken alone, are retained scarcely at all, while fat and protein are retained for long periods. To what extent this knowledge should influence our dietetic habits it

is difficult to decide, but it is an excellent argument in favour of the simple French breakfast. On the other hand, in view of the fact that special arrangements have been made for the digestion of carbohydrates during retention in the gastric reservoir, there seems to be every provision for the eating of a mixed diet.

When the food in the stomach becomes largely digested and its acidity over 0.2 per cent., reverse peristalsis and regurgitation of the duodenal contents takes place to prevent, as we have seen, excessive acidity. This we must now take as a fact and we shall see that such reverse peristalsis is also a physiological process in the large intestine. It has, indeed, been described in a case of intestinal fistula as existing in the small intestine.

For diagnostic purposes, however, the time of emptying of the stomach is of great importance. Food begins to leave the stomach at once, provided it is mainly of a carbohydrate nature, as the ordinary bismuth meal by which such an investigation has been made usually is. Discharge continues for some time, but at the end of three hours the stomach should be empty and degrees of retention can be estimated by finding the time taken for complete emptying.

Evidence of delay is best obtained by observation with X-rays of the time of evacuation of a bismuth meal. Simple means will also give a large amount of information. For example, the giving of a charcoal biscuit the evening before a test meal (see page 225) is often used. The presence of charcoal in the stomach when the test meal is drawn off in the morning will be evidence of retention. Similarly, the presence of a large amount of fluid in the stomach during resting periods, its large size, and the presence of splashing (seen when a stomach tube is passed) all indicate retention. The administration of drugs such as salol which are not absorbed until they reach the intestine is also used as a test.

CHAPTER XXVII

MOVEMENTS OF THE INTESTINE

Physiologists recognize three kinds of intestinal movement: peristalsis—by which the food is moved along; segmentation—by which it is broken up and absorption facilitated; and pendular movements. The clinician is interested chiefly in peristalsis, as deficiency in this respect (causing constipation) is, with the common cold, probably the most common complaint amongst modern peoples. We have seen that intestinal stasis may interfere unduly with the emptying of the stomach, but what is just as important is the toxic absorption which may also result. Normally, the small intestine is the region from which the products of normal digestion are absorbed, but if the contents stay there too long then putrefactive products are produced and absorbed to the great disadvantage of the individual. Such intestinal stasis is, however, usually secondary to failure of the large intestine to move on its contents.

So far as the small intestine is concerned, excessive peristalsis most commonly interests the clinician. Such peristalsis may be brought about as the result of irritation of the mucous membrane lining the gut. This sets up excessive muscular action, just as we have seen that an ulcer may produce excessive contraction in the stomach. The irritant may be the result of the ingestion of food substances, e.g. green gooseberries, or it may be bacterial, as in typhoid fever. In each instance the excessive peristalsis and subsequent diarrhœa may be looked upon as Nature's method of expelling the irritant. Advantage is taken of this suggestion in the treatment of early or suspected ptomaine poisoning in which a brisk purgative (castor-oil is the favourite) often averts more serious symptoms. It should be noted that unripe fruit which causes irritation of the bowel also causes diarrhœa in virtue of its indigestible bulk which causes distension and stimulation of the bowel. That muscular movement may be so stimulated is well known and it may be due to fluid, gas or food. The effect of distension may readily be seen in a piece of rabbit's intestine kept warm in saline and oxygenated. The bowel is seen to be quiescent, but on introduction into its lumen of a distending object, movement will be seen to commence and to drive on the obstruction. It will be seen, too, that the wave of contrac-

tion is preceded by a wave of dilatation, which is as much an essential part of the peristaltic movement as the constriction. This has been known as the Law of the Intestine. It will also be seen that if the object is a little too large for the lumen, if there is insufficient lubrication or if a kink is made in the gut, special efforts are made to drive on the object. Thus we see a succession of waves commencing a few inches from the obstruction and apparently gathering in intensity as they reach the object. There is a rest period and then a further succession of waves. A similar state occurs pathologically when there is obstruction in the intestine, e.g. a carcinoma, where local hypertrophy of muscle immediately in front of the obstruction takes place from the excessive amount of work and this indeed is looked for by the surgeon when trying to find the obstructed point. The wave-like character is necessitated by the characteristic of smooth muscle which is refractory, i.e. does not respond to a stimulus until the previous contraction has passed off. The paroxysms so characteristic of colic, are due to the groups of waves and the rest period. This is seen in biliary colic caused by the presence of a gallstone in the bile duct, renal colic due to a stone in the ureter or intestinal colic from stimulation of the intestine. These intermissions are an important diagnostic factor in differentiating the conditions from inflammatory lesions.

In some instances, especially spasm of the large intestine, the pain appears to be due to very slow waves rather than to a succession of waves. In dysentery, for example, the waves can be appreciated by the patient as travelling slowly along the course of the large intestine. The slow waves are more commonly looked on as in the nature of a spasm or tetanus, although they cannot be imitated outside the body by experiments on smooth muscle. They are almost always confined to the large intestine, the pain is intense and may simulate various other conditions if not recognized. They are quite frequent as the result of the excessive use of purgatives or in colitis, and in such cases, if the patient is thin, the colon in the iliac fossa can often be felt to contract under the hand and feels like a sausage. Not infrequently this is mistaken for a tumour or a fæcal accumulation. Atropine is almost a specific in such cases, just as we noted in pyloric spasm, and morphia is commonly necessary for immediate relief. Treatment of such conditions consists in giving the individual a diet with little or no indigestible material until the irritation has passed off, a treatment which throws considerable light on the physiological principles which apply to intestinal stasis and constipation.

Intestinal stasis must always be considered physiological in so far that in a large number of people it is impossible to avoid it unless special steps are

taken, as it is largely the result of the assumption of the erect posture in man and in many the necessary adaptations are deficient.

Intestinal stasis is the result of inefficiency of the large intestine in passing on its contents. In man the large intestine acts only as an organ for the absorption of water and for the excretion of certain salts such as sulphates and phosphates and the salts of calcium and magnesium and iron.

This latter fact is taken advantage of in the common saline purgatives, e.g. magnesium sulphate. On reaching the large intestine these salts retain water which would normally be absorbed, or if sufficient water has not been ingested, cause water to osmose through the bowel wall to distend the gut and stimulate it, whilst at the same time it dilutes its contents. In this way the salt hastens evacuation.

It seems possible that phosphates have a special relation to intestinal movements. We know that the oral administration of phosphates have a greater laxative effect than would be expected and when di-sodium hydrogen phosphate (Na_2HPO_4) is injected intravenously the stimulating effect on the intestines is very striking. This beneficial effect may also be demonstrated on pieces of isolated intestine.

There is no doubt that undue concentration often results from an inadequate intake of water. This should preferably be taken before meals to interfere as little as possible with digestion. As the bowel contents are normally fluid at the exit from the small intestine it is obvious the more fluid they are at this point the more they will be when they reach the pelvic colon. The beneficial effect of a large tumblerful of water before breakfast is well known and indeed at watering-places individuals can be persuaded to take as much as twenty ounces, although they would never think of doing so at home. The fact that it is taken before breakfast is of great importance as at this time the small intestine is empty and the water passes through it so rapidly that there is little time for absorption. Such a quantity of fluid could not have the same benefit if taken with a meal, as it is delayed at all stages, although actually absorption is somewhat facilitated by the taking of reasonable amounts with the food. The fluidity of the bowel contents may, however, be improved by adding to the diet a substance which is fluid and not absorbed. Such a substance is liquid paraffin which is recommended by Arbuthnot Lane, a leading authority on this subject. The paraffin simply acts as a diluent and lubricant.

Surgical procedure and anatomical dissection indicate that as the result of the erect posture certain parts of the bowel are liable to kink or to constriction by peritoneal bands. Lane's kink and Jordan's band are well-known entities.

There can be little doubt, as emphasized by many of the leading surgeons, that these are the unfortunate results of our heredity. If not too severe they may be greatly mitigated by proper dietetic and other means such as exercises and medical treatment on physiological principles, and this is all that is necessary. In severe cases surgical interference and possibly anastomosis between the ileum and pelvic colon may be required.

What has been said above regarding the fluidity of the bowel contents is of great physiological importance, but so also is the nature of the food, as has been briefly referred to on page 188. It is obvious that it is much more difficult for the bowel to propel a soft pultaceous mass than one containing some reasonably hard particles of cellulose. The average diet contains too little indigestible material or roughage. In our civilized diet the majority of carbohydrates taken have had their cellulose removed or reduced to powder, as in white flour, which in some form or other forms a very large part of our dietary. Additional cellulose is necessary and is best taken as fruit and vegetables. From this point of view faulty mastication of, say, meat adds to the solid contents of the large intestine and it is well known that individuals with defective teeth, if they do not suffer from indigestion due to pyloric spasm, often suffer from looseness of the bowels. Insufficient mastication would of course be a most unphysiological treatment to recommend as it is so apt to upset gastric function and, of course, would be a most wasteful procedure. The influence of the diet in spasm of the colon has been referred to above and indicates clearly the effect of roughage in stimulating the bowel.

In any consideration of the cause of constipation or diarrhœa the individual case has to be considered, for the whole intestinal tract is influenced by the general state of the body and habits. Diarrhœa may be a manifestation of general irritability and excessive secretion by the mucous membrane. Of such a nature is mucous colitis, where local treatment is of little avail without general measures. Similarly, constipation may be due to general lack of secretion and body tone as in the aged, the anæmic, the melancholic or in the febrile states. These may be further accentuated by particular substances, as, for example, calcium of milk or hard water which reduce the normal secretion. Notoriously too, sedentary habits are liable to cause constipation from lowering of the general tone and especially of the tone of the abdominal muscle. The latter if permitted to grow slack allows the viscera to become displaced and by intensifying kinks or causing sagging of the large colon, renders the work of the intestinal muscle more difficult.

Undoubtedly, too, the physiological calls of nature are often neglected.

Evacuation of the bowel should take place after breakfast, a time which for most of us is the most occupied of the day. A call is normally brought about by the so-called ileo-colic reflex by which the ileo-cæcal valve is considered to open and allow the passage of the contents of the ileum into the large intestine when the stomach is filled. That the mechanism, however, is not so simple and probably depends on a co-ordinating mechanism by which all the bowel contents are moved on, is seen by the fact pointed out by Leathes that the reflex persists in man when the ileo-cæcal region has been removed surgically. It may be that the reflex is "conditioned" in nature. Neglect to evacuate the rectum when loaded tends to cause atony of that part of the bowel which becomes insensitive. Regular habits in this respect are therefore essential.

As has been said, stasis may be considered largely the result of the assumption of the erect posture and the results of the stasis can be best appreciated if we glance at the functions of the large intestine in lower animals when the indication of its real function will be seen. This was well described by Barclay Smith in 1902 and has subsequently received much attention. In herbivorous animals the colon and particularly the cæcum are well developed and serve as organs wherein the cellulose is broken down by bacteria, for normally cellulose is not attacked by the digestive enzymes. To facilitate the entrance of the food into the large cæcum there is reverse peristalsis in that which corresponds in man to the ascending colon. This anti-peristalsis persists as a relic in man. At the same time, too, it is necessary that the ileo-cæcal valve should be efficient to prevent the food being driven back into the small intestine, while to deal with any bacterial leak we have developed the well-known lymphoid nodules or Peyer's Patches at the lower end of the ileum. With the assumption of the erect posture the work of the muscle of the ascending colon becomes appreciably increased and it may break down, with the result that the ileo-cæcal valve becomes incompetent, and although this valve retains its efficiency, mere stasis in the cæcal region will result in food remaining too long in the ileum. As the result of bacterial decomposition taking place in this region, the toxic products are absorbed and the effects of these have been emphasized, particularly by Metchnikoff and subsequent writers. It is well known that the latter conceived an idea of counteracting the bacteria of decomposition by the addition to the diet of other bacteria which would antagonize them. Obviously, this method is much less physiological than those which promote the activity of the intestine, as indicated above. A great deal, however, of what has been written regarding intestinal stasis is really true, although exaggerated claims have been made in relation to its being the cause of specific diseases. There is not the

slightest doubt that in this condition there is general depression, lessened mental and bodily vitality and reduced power of withstanding infection. The effect of short-circuit operation in some chronic infections, such as pyæmia, tuberculous joints, to give examples only of what have come to the author's personal notice, is sometimes nothing short of marvellous, and anyone who has seen the beneficial effects of colon treatment supplemented by exercises, such as that elaborated by Chalmers Watson and many others for a variety of different chronic conditions, cannot but be impressed with its efficiency in the many conditions to which no actual disease label can be attached, quite apart from definitely chronic pathological states.

So important are the movements of the intestines clinically that one must be possessed of means of estimating their efficiency. In the first instance it must be said that daily evacuation of the bowels is an indication which cannot be relied on. The patient may give a history that this does occur, but the amount excreted may be insufficient or perhaps should have been got rid of some days before. Further, when fæces become packed and dry in the pelvic colon they tend to set up irritation which may even bring about diarrhœa which, from the point of view of the patient, will mask the constipation, although the passage of hard lumps during this so-called diarrhœa which alternates with the constipation indicates the real condition to the clinician. The consistency of the motion is then a better indication as it depends on the duration of retention in the colon.

Much the most satisfactory method is by X-rays as introduced by Cannon, in which the times taken by a bismuth meal to reach different parts of the intestinal tract is noted. The method generally, of course, can only be applied to those parts of the intestinal tract which have a fixed position. It cannot therefore be applied to the small intestine, but fortunately lends itself to use in the large intestine where it is most necessary. A bismuth meal is seen to appear in the ileo-cæcal region four hours after the meal has been taken; this is preferably in the morning, so as to have reached the hepatic flexure in six to seven hours, the splenic flexure in ten hours and the pelvic colon in twelve hours. By this means, also, local points of constriction may be observed and any special abnormality in the position of the colon noted.

Often, however, X-ray apparatus is not available and then a purely clinical examination has to be relied upon. Charcoal biscuits may be given and the time taken for the charcoal to be evacuated noted. Palpation and percussion of the left iliac fossa should reveal an empty colon after the bowel has been evacuated and colon lavage or an enema should give little or no result. In the same way

there should be no undue dullness or fullness in the cæcal region. These signs, together with inspection of the stools, give a useful indication as to whether or not the activity of the large intestine is reasonably normal.

A great deal of information can also be acquired from investigation of the bacterial flora of the gut obtained preferably after a wash-out. Little attention as yet has been paid to this aspect of physiology, very largely no doubt because few physiologists have a good training in bacteriology. It is, however, impossible to admit the fact of the bacteria playing a considerable part in the economy of the lower animals, such as the herbivora or even as low down as the molluscs, and yet ignore their presence in man. We have, indeed, special lymphoid tissue scattered along the intestinal wall, particularly at the lower end of the ileum and apparently intended to deal with any bacteria which should escape from their usual habitat in the large intestine. If the intestinal bacteria are in excess they get into the blood-stream and as the evidence collected by Kidd shows, are excreted by the kidney which must be looked upon as a normal channel of excretion, although it is difficult admittedly to see how the bacteria pass through the membranes unless they cause partial destruction. It may be that they cause destruction too small to be significant. It is only when such a comparatively harmless bacterium as bacillus coli is excessive that it has any pathological significance in the intestine or in the urine. According to Chalmers Watson the normal stool from an intestine not unduly stagnant and loaded with bacteria should be odourless.

We have been familiar with the fact that typical pathological bacteria find their way to the kidney from the intestine, such as bacillus typhosus, and that nephritis is a common complication of scarlet fever. It is then not more difficult to consider that this may be also a normal channel of excretion. There is, indeed, much evidence which suggests that chronic nephritis may in many cases be produced by an excessive excretion in this way, necessitated by chronic intestinal stasis and infection.

CHAPTER XXVIII

PHYSIOLOGICAL AND PHARMACOLOGICAL PRINCIPLES IN RELATION TO COMMON GASTRIC AILMENTS

In few branches of medicine is there such confusion as in regard to diseases of the stomach, for each author has his own classification. To realize the truth of this statement one has only to pick up half a dozen textbooks, and attempt to get from them a clear conception of what is commonly called indigestion or dyspepsia. Far be it from the intention of a physiologist to attempt to rectify what is certainly a difficult position, yet there can be no doubt that in such classifications much of the confusion is due to failure to appreciate the gradual transition from one so-called disease into another.

Gastric pain or discomfort is usually the predominating symptom, less commonly there is perforation or hæmatemesis. From the evidence of operations under local anæsthesia it is clearly evident that only the abdominal wall requires to be anæsthetized. The stomach does not feel ordinary sensation. There is also excellent proof that gastric pain, provided there is no inflammation of the parietal peritoneum, is the result of muscular contraction and tension (see "Sensation"). The realization of this fact alone throws light on the general gastric symptomatology.

Gastric pain will result from anything which obstructs the emptying of the stomach by introducing a resistance in the region of the pylorus, which interferes with the contraction of the musculature or which by irritation causes muscular spasm.

Increased Resistance.—This may be brought about by pyloric obstruction due to adhesion, or cicatrix formation after ulcer, or congenital muscular hypertrophy. It may be merely functional as the result of abnormal contraction of the pyloric region. How the abnormal contraction may be brought about is indicated in the previous chapter. We may look upon the pylorus as not allowing articles to leave the stomach until of a reasonably fluid consistence. Further, it will not allow excessive hydrochloric acid to reach the duodenum, and will not pass on food to the small intestine under conditions of emotional emergency, or when there is inflammation lower down. This latter is in the nature of a protective reflex. Here we find the explanation of indigestion

caused by the gulping of food, since the coarse particles cause the pylorus to contract.

Hurst, to whom we owe much regarding the sensibility of the alimentary canal, distinguishes between an actual spasm of the pyloric sphincter and achalasia or failure of the pylorus to open normally. In the latter instance he considers the pain to be due to contraction of the pyloric antrum which attempts to force its contents through the closed pylorus.

In the protective reflex spasm or in achalasia of the pylorus we have the physiological explanation of the dyspepsia secondary to inflammatory conditions such as chronic appendicitis, although the disease in the organ may be insufficient to produce local appendicular symptoms. In the dyspepsia resulting from emotional states such as worry and anxiety, or in excessive mental work, we have no doubt a relic of the fact that animals under such emotional stress do not partake of food, the alimentary canal being brought to a standstill by contraction of all the sphincters and relaxation of the bowel wall. See "Sympathetic-parasympathetic Balance." In these conditions the secretion of HCl is often reduced or there may be excessive neutralization where the relaxation is more marked than the sphincteric contraction. An analogous condition is produced in acute disease which brings into operation the same mechanisms which were intended for natural emergencies such as occur in fighting. We have a similar adaptation of the natural mechanism of exercise to the requirement of disease in the essential supplies of oxygen and elimination of carbon dioxide from the body and there is a similar output of energy from the storage areas into the active circulation. In all such conditions associated with undue contraction of the pylorus, whether of the sphincter or the antrum, there is a tendency to increased acidity of the stomach contents or hyperchlorhydria. The pyloric contraction is intensified by the hyperchlorhydria itself. The primary condition may be determined by means of the fractional test meal (see the previous chapter). A primary spasm or achalasia will show increased hydrochloric acid, and a lack of neutralization, there being no increase in the total chlorides. A true hypersecretion, on the other hand, is characterized by a rapid rise in the acid and total chlorides. The amount of acid will depend on how much neutralization has taken place, while there is also a rise of alveolar carbon dioxide (*q.v.*). Hyperchlorhydria is then not a necessary accompaniment of hypersecretion and *vice versa*. Hyperchlorhydria, acidity, acid dyspepsia due to pyloric spasm and subsequent lack of neutralization is one of the most common forms of functional disorders of this kind, and is, as we shall see, generally associated with ulcer.

A true hypersecretion may be brought about. Here we must remember the normal mechanisms by which secretion occurs. If the reflexes generally are exaggerated it is to be expected that reflex secretion of gastric juice will be similarly affected. In such cases if the food, say as a result of faulty mastication, is detained in the stomach, its retention may, depending on its nature, bring about excessive secretion. In the same way substances which will produce gastrin or histamine are inclined to cause excessive response. In this relation Lim has clearly shown that histamine is a powerful gastric stimulant, easily produced from decomposing proteins. It is seen from such experiments and from the examination of "normal" men, or at least men without any stomach complaints, that a great increase in gastric hydrochloric acid may occur without any discomfort. It may indeed be said that to consider the symptom as due to hyperchlorhydria *per se* is like considering sputum to be the cause of a chest complaint.

The increased resistance may be the result of increased *vis a fronte* from stasis in the bowel lower down. Whether this stasis is of such a degree as to impede the emptying of the stomach in all cases is very doubtful, but it is certain that much indigestion is cured by simple attention to the bowels. No doubt the effect of the absorption of toxic substances on the gastric secretion and tone play a part, while it is common experience that constipation causes lack of appetite, insufficient salivary secretion, a nasty taste in the mouth, and a foul breath, although indigestion may not actually supervene.

The continuation of obstruction may eventually bring about relaxation of the gastric wall, the clinical condition known as gastric atony, which is dealt with below, and in which the stomach is dilated and incompletely empties itself. The normal resonance is increased and splashing may be elicited. Once the lack of adequate emptying is established the nature of the condition tends to make it progressive and the feeling of weight becomes worse and in extreme cases the lower border of the stomach may extend into the pelvis. It is to be noted that the pain in such cases is quite different from that of gastric ulcer, which is usually much more acute. In atony, however, the pain is often more a sense of heaviness and fullness, which is also further aggravated by interference with the musculature of the stomach. The retention tends to bring about bacterial decomposition and increasing accumulation of gas in the fundus, which further aggravates the condition and may cause intense discomfort.

Not infrequently the pain is attributed by the patient to the heart, and on this is based the dictum of an old physician, "When a patient complains of his heart, examine his stomach." The pain, as may be expected, is often in pro-

portion to the amount of food taken, especially if the latter is of a decomposable nature, e.g. carbohydrates, and follows immediately after meals. The reputation of the coarser vegetables in causing flatulence would appear to depend on the retention of carbohydrates, brought about by the effect of their coarseness on the pylorus. Eructations, as would be expected, relieve the pain, but vomiting is infrequent, because, in the nature of things, it is impossible, owing to the general weakness of the musculature. Nor is there a local point of tenderness as there may be in ulcer. Unfortunately the enlargement of the stomach wall frequently means that the individual does not feel satisfied until considerable quantities of food have been taken, a circumstance which makes such patients very difficult to control, as the reduction of the amount of work to be done by the stomach is an essential part of the treatment.

Interference with the Musculature and Tension.—This may occur secondarily to obstruction, but may be brought about by over-eating if continued, although there is ample evidence that the stomach, like any other organ, may adapt itself to considerable overwork. Food liable to decomposition and production of gas is a frequent source of such indigestion. The amount of bread and potatoes consumed by some individuals is enormous, and the cutting off of those two articles of diet often brings complete relief. The accumulation of gas interferes with the power of the muscle to drive on the contents, and if continued, the condition of gastric atony tends to be produced as in pyloric spasm. If the interference with the musculature is the primary cause of the stomach disturbance there is evidence that in such cases excessive neutralization through the patulous pylorus may occur.

Irritation.—Gastric irritation may be general or localized. It not only brings about muscular spasm, but also vomiting, which often relieves the condition, at least temporarily. General irritation is seen in acute gastritis, in which the whole organ is probably affected. Commonly the pylorus is closed, and the stomach contents do not escape. The presence of bile and large amounts of fluid in the stomach suggest that excessive regurgitation through the pylorus has taken place. A so-called "bilious attack," as explained above, appears to be of this nature. The pain of acute gastritis is, as would be expected, somewhat generalized.

More localized irritation occurs in gastric and duodenal ulcer. It must be understood that these conditions are by no means so clearly defined as their names suggest. To obviate any misconception Continental writers have introduced the term "juxta-pyloric" to include all ulcers in the pyloric region.

These conditions have long been recognized as pathological entities which

present certain symptoms. These are pain or discomfort in the epigastric region with possibly tenderness, which according to Mackenzie is related to the site of the ulcer. The pain, as stressed by Moynihan, bears a remarkably constant relation to the time of taking food. If the ulcer is gastric the pain comes on within an hour of taking food, and later disappears. If the ulcer is a duodenal one the pain is worst when the stomach is almost empty, two or three hours after food, and then persists until more food is taken. In gastric ulcer vomiting relieves the pain, and hæmatemesis may occur, or the existence of bleeding may be shown by the presence of blood in the stools. The clinical history is often sufficient to make the diagnosis clear. The relationship of ulcer to the hydrochloric acid of the stomach is of considerable importance in the progress and treatment of the condition.

The amount of free hydrochloric acid in the gastric juice varies greatly in such cases. It may be normal or even less, though it is usually more. From what has been stated in the previous chapter the hydrochloric acid content will depend on the amount of neutralization which has taken place. We do know experimentally that free hydrochloric acid in the stomach delays the healing of the ulcer. All the evidence points to the fact that the pain is due to gastric spasm brought about by the presence of the ulcer and accentuated by the acid. Relief is given by alkali which neutralizes the acid. The mere presence of an ulcer which for some reason does not cause the stomach to go into spasm, does not cause pain. In some gastric ulcers there may be no symptom until perforation has occurred.

The recognition of the fact that ulcers of the alimentary canal bring about excessive muscular action is by no means new. In infective conditions of the colon, e.g. acute dysentery, which are so frequently associated with ulcer, the muscular contraction amounts to a severe tenesmus. It is of such an excruciating nature that those who have experienced it are not likely to forget it. The presence of colicky pains confined to one region has long been used as a diagnostic sign of a persistent ulcer after dysentery.

The methods adopted by some surgeons for the cure of these gastric conditions are of great interest in this connection. Gastro-enterostomy, in which the jejunum is attached to the stomach, was at first fashionable. Later this was combined with local treatment of the ulcer, by cauterization or excision, as in Balfour's operation. More recently Moynihan, a leading exponent in the surgical treatment, recommends partial gastrectomy as the best operation. Jejunostomy is sometimes performed, so that the patient can be fed directly into the small intestine, and various other methods have been tried. Experienced sur-

geons are not as yet in complete accord regarding the best operation and the number available indicates that a panacea has not yet been found. When the physiologist considers the variety of conditions concerned he does not expect to find a universal surgical panacea. From a study of the operations referred to above, it is evident that each in turn brings about a separation of the ulcer and hydrochloric acid, and naturally gastrectomy is the most efficient, as by it the ulcer-bearing area and no doubt a large number of the acid-producing cells are both extirpated. Moynihan seeks to put aside this obvious observation by the suggestion that a cell of the gastric mucous membrane "is born, lives and dies in an acid medium." Physiology has not yet discovered any cell which is capable of growing or even performing its functions in an acid medium. Although the superficial cells of the mucous membrane can withstand dilute acid (the various influences which prevent the gastric mucous membrane from being digested are as yet incompletely understood), certain it is that the tissues at the base of the ulcer and the deep part of the mucous membrane where the cells are dividing are normally in an alkaline medium.

That the benefits of successful gastro-enterostomy for gastric ulcer (for there have been successful cases) depend on neutralization of the hydrochloric acid is shown by the fact that the hydrochloric acid in the stomach is reduced and the symptoms may disappear, although the food may continue to pass not through the new opening but through the pylorus as the muscular arrangement of the stomach tends to make it do. Unsuccessful cases of gastro-enterostomy, however, do not show this neutralization. Let it be clearly understood, however, that where there is organic pyloric obstruction, surgical measures which prevent the retention of food in the stomach have a very real value, they may be of advantage even in functional spasm, for the difficulty in getting individuals to carry out medical treatment for the necessarily long time when perhaps it is necessary to pursue some avocation—is no small one. It must also be remembered that mere section of the stomach wall would tend to cause cessation of the spasm of the musculature and give relief, while, as we shall see, it will temporarily break the vicious circle.

Surgery has proved without doubt the association of ulcer with hydrochloric acid in the stomach. The fact that the acidity is often subnormal does not affect the conclusion which both clinical and experimental evidence shows, namely that it facilitates the formation and delays the healing of ulcers. The actual agent responsible for the formation of the ulcer is a matter for the pathologist. More and more evidence is being brought forward to indicate that it is the result of local septic infection such as we may get in any other

part of the body. This may originate in injury or transference of septic emboli from elsewhere, e.g. the teeth. Local conditions such as faulty dietetic habits, increased sympathetic action (see "Sympathetic-parasympathetic Balance"), bringing about an interference with the normal control of the musculature, and excessive hydrochloric acid undoubtedly predispose and prevent the healing which normally occurs, otherwise most of us would be victims.

We are familiar with the overworked individual (four physiologists have recently suffered) who, pushed for time, eats a hurried light lunch in his laboratory, possibly while actually working, who develops all the signs and symptoms of ulcer and who recovers when his repast becomes more physiological. Unfortunately clinicians have done little as yet to unravel the details of the faulty dietetic habits responsible. We know also too little regarding clinical variations in the secretion of the alkaline juices of the duodenum which normally neutralize the acid. It is evident that any diminution in secretion will necessarily lead to increased free hydrochloric acid in the stomach, even if secretion of the latter is normal.

Surgery indicates that the hydrochloric acid in the stomach is responsible for delay in the healing of the ulcer, but further, we have seen that normally the acid is neutralized by regurgitation of the duodenal contents. It is evident, then, that undue closure of the pylorus must indirectly prevent this neutralization. We have, then, in gastric ulcer a vicious circle, an ulcer acted upon by hydrochloric acid causing spasm of the pylorus, this spasm preventing normal neutralization and an excessive amount of acid being allowed to accumulate and possibly extend the ulceration. On physiological principles we must break this circle by reducing the amount of acid secreted or neutralizing it or by preventing the pyloric spasm.

The essence of treatment is the provision of the necessary protein in a way not calculated to stimulate acid secretion and in a physical form in which it passes easily through the pylorus. At the same time food must be of such a nature that it stimulates the secretion to a minimal extent in virtue of its chemical constitution. Meat extractives and highly flavoured dishes should be therefore forbidden. In treatment, fatty foods which tend to inhibit gastric secretion are to be preferred and with this in view a teaspoonful of olive-oil or cream may be given before meals. White of egg, milk, and bread can supply the majority of the proteins required by the individual, while atropine is also administered in view of its action in reducing the secretion. At the same time alkalies are to be given to neutralize any acid which has been secreted. It is true that alkalies in small amount, especially if given before food, tend to

cause an increased secretion of gastric juice and this crude fact has been employed by surgeons against the rationale of the alkaline treatment. These criticisms may be true of the old sodium bicarbonate treatment of thirty years ago. Elementary chemistry teaches us, however, that the best neutralizing effect is to be expected from the alkaline salts of the divalent or trivalent metals, e.g. magnesium and bismuth, which, further, do not have the same stimulating effect as sodium salts. Of the two, magnesium is to be preferred, as it has a mild laxative effect which is an advantage, while bismuth tends towards constipation. The work of Crohn and Bennett also shows that alkalies, to be efficient, should be given some time (one-half to two hours) after food, to exert their neutralizing effect to the best advantage.

In the light of what has been said the rationale of the stock remedies of the last generation for gastric conditions becomes evident. Milk and soda as a complete dietary was commonly advised. Later on bismuth and soda became more fashionable, the bismuth being supposed to coat the ulcer. The routine treatment of gastric ulcer where there was no actual bleeding was, frequently, two ounces of milk and water two-hourly, and is in nature the same thing. The fact that the administration was every two hours materially assisted in the reduction of the acid content. This no doubt, as the physicians used to say, prevented too great an accumulation of milk clots in the stomach. By confining the patient to bed his calorific requirements were reduced to a minimum. These treatments were directed towards lessening the irritability of the ulcer, and neutralization of the hydrochloric acid, and while quite effective for new cases (where such neutrality was quite sufficient to bring about a cure), they lost their reputation when applied to the treatment of severe chronic cases.

Hurst offers an interesting explanation of the relief of flatulence brought about by the administration of sodium bicarbonate which by interaction with acid increases the gas in the stomach. He considers that the pain is due to the attempts of the pyloric antrum to force its contents through a closed pylorus and that the production of carbon dioxide from the bicarbonate assists by increasing the internal pressure.

Pyloric spasm is reduced by the administration of atropine which reduces secretion. That the whole action is not wholly due to diminished secretion is seen by the fact that although the free acid is reduced, the chlorides continue to rise slowly, since the acid as secreted becomes neutralized by duodenal regurgitation. The atropine or belladonna is often given in a little olive-oil or cream before the meal.

All these features of treatment were incorporated in the elaborate dietary of

Sippy, which is scarcely possible except where there is adequate supervision. Less elaborate methods, such as those of Bolton and Hurst, are quite adequate.

Recent insurance statistics of cases of ulcer in medical men, who presumably carry out this treatment efficiently, indicate an advantage in favour of medical treatment. This is founded on the foregoing physiological principles and accompanied, no doubt (and this is essential), by rectification of the primary cause of the condition, which is usually dietetic.

There are many gastric pains which are often described as dyspepsia, but as yet we have very little information regarding them. The clinical differentiation is often very difficult. It is best to study the pathology and physiology of such cases in the light of what has been written above.

It has been emphasized by Keith that many of our greatest writers have recorded their stomach complaints, e.g. Carlyle, Darwin, Huxley, Spencer. Indeed he suggests that in this sense the stomach, which is an organ essentially designed for the large intake of energy necessary to exercise, is antagonistic to the brain. Illustration may be given, for the purpose of indicating how the gastric mechanisms may readily become upset and of showing how closely allied are physiology and pathology.

Consider an individual leading a somewhat exacting sedentary occupation. His meals are hurried and probably badly masticated, with the result that food not suitable to pass through the pylorus is taken into the stomach. At meal time he may think of all manner of things other than his food and may even read serious literature and it will be evident that he loses all the advantages of psychical and of appetite secretion. His food takes longer to digest as the result. Possibly he consumes articles which are difficult to digest and may take excess of tea or coffee. There is evidence that during intense mental work the sympathetic nervous system is active (see also "Sympathetic-parasympathetic Balance"), a fact which still further interferes with the emptying of the stomach, exactly as we know does severe exercise. The first stage in the onset of dyspepsia is probably, then, simple pyloric spasm which most of us may experience from time to time, as a result of temporary indiscretions of the nature indicated above. Associated with pyloric spasm we have the failure of the normal regurgitation of the duodenal contents and the accumulation of hydrochloric acid which tends to be increased further from the action of the putrefactive products. This we know clinically as the stage of hyperchlorhydria, during which there is great liability to ulcer.

Subsequently, there is retention of the stomach contents, bringing about dilatation and gastric atony, with possibly actual degeneration of the acid-

producing cells. As would be expected at this stage, since the muscle has failed, the symptoms are not particularly acute, indeed there may be a sense of fullness rather than of pain. The exact stage when dilatation sets in appears to depend on the general state of the individual, and it will be remembered that gastric pain is notoriously depressing. The importance of the mental state cannot be over-estimated. Langdon Brown gives an instance, for example, in which the atony was clearly associated with the mental effects of air raids. Once such a condition is begun and the muscle begins to lose tone, there is a tendency for the emptying of the stomach to be less and less complete, while fermentation becomes super-added and by producing increased distension aggravates the condition.

It will be realized that variations of this course may occur. During the hyperchlorhydria the stomach may receive an injury and ulceration be brought about. As we have seen, the hyperchlorhydria tends to prevent the ulcer from healing. Or again, the scarred tissue of healed ulcers may lead to stenosis which will bring about dilatation.

Whether all cases of dilatation and increased acidity are brought about in this way is not quite certain, but undoubtedly such a sequence of events is extremely common and it must be emphasized that no amount of medical treatment can compensate for faulty dietetic habits. After all, the pathological conditions are but the result of disturbed physiology.

A study of gastric function in relation to symptom production would be of advantage. Much can be done by the general practitioner in correlating faulty dietetic habits with symptoms. These are the result of a disturbed physiology and no matter what treatment is adopted none can be of real value if the patient is allowed to lapse into his old habits. Here surgical measures have a moral advantage, since the thought of subsequent operation acts as a corrective. It is necessary that the physician should seek out the primary cause of the condition, and this is true clinical research. More detailed examination by X-rays, at surgical operation, and post-mortem examination, brought into relation to symptomatology, would also be of the greatest value. Much more light is needed on the various stomach-aches, to which we creatures of a so-called civilized diet and habits are heir.

CHAPTER XXIX

BLOOD-SUGAR AND PANCREATIC EFFICIENCY

The modern treatment of diabetes by insulin and its control by investigation of the blood-sugar makes this determination of much greater clinical interest than before, and it is a good example of the influence of clinical medicine on pure physiology.

We know there is a normal blood-sugar level just as there is a normal urea or carbon dioxide level in the blood which is essential to life. The level of the blood-sugar varies normally from 0.08 to 0.18 per cent., depending chiefly on the amount of carbohydrate being absorbed. One must suppose that this concentration is that which is necessary for the satisfactory working of the vital organs. If the blood-sugar in a starved animal is made to fall by insulin injection below 0.04 per cent., it goes into convulsions and dies. Restoration from the convulsions may be brought about by the injection of glucose. This is taken advantage of in the standardization of insulin, the strength of which is estimated by its effect on a rabbit of given weight and under given conditions. Should there be an amount of sugar in the blood above 0.1 per cent., the excess is excreted by the kidney. This percentage is often referred to as the "renal threshold" for sugar. It is not until the blood-sugar has reached about 0.2 per cent. that sugar may be detected in the urine, by the common tests, such as that of Fehling. Hence it is that the finding of sugar by such a test is clear evidence of abnormality. As soon as the blood-sugar gets beyond 0.2 per cent. there is a marked decrease in the power of the kidney to retain sugar (Hamburger), and a much greater proportion of the excess appears in the urine. This point has been termed the "leak point" of the kidney, and is of important clinical significance. It will be evident that should the threshold be reduced, although the blood-sugar is not excessive, there will be glycosuria, and the production of the condition known as renal glycosuria, which not infrequently results from impairment of the kidney by disease, such as nephritis. The mere presence of sugar in the urine does not necessarily indicate hyperglycæmia, i.e. excessive sugar in the blood, and in such circumstances should steps be taken to reduce the blood-sugar further by injection of insulin disastrous results may ensue, as indicated above. Actually the stores of sugar or glycogen would

first require to be used up, for it is more difficult to produce convulsions in a well-fed rabbit than in one which has been starved.

A rise of blood-sugar will occur (1) if an excessive amount of sugar be absorbed from the alimentary canal, and (2) if the sugar is insufficiently used.

Here it perhaps should be said that the term sugar is held to include the copper-reducing monosaccharides.

Should the hyperglycæmia and consequent glycosuria be due to excessive sugar ingestion this will at once be indicated by the diet, but it is evident that if there is any deficiency in the sugar utilizing powers of the individual, less sugar than normal may be required to cause the glycosuria. This has been applied to the diagnosis of diabetes. Normal individuals should be able to assimilate one or two hundred grammes of glucose without any sugar appearing in the urine and some individuals can use as much as 500 grammes. So many factors, however, such as the absorption, the habit of the individual, may influence the result that this test, according to Macleod, cannot be relied upon. The assimilation power as it is called has for many years been of considerable value in the dietetic treatment of the diabetes, and indeed was the basis of treatment prior to the discovery of insulin, and is still used in the treatment of milder cases of the condition. The patient's diet is regulated so that the carbohydrate intake is just short of that which causes glycosuria and he can as a rule be taught to make simple urine tests for his own guidance. The danger of cutting off carbohydrate suddenly will be alluded to below.

The clinical test now commonly used for the ascertaining of the power of the body to deal with carbohydrate is the determination of *blood-sugar curve*. In the test 50 to 100 grammes of glucose are given in water by the mouth and samples of blood are taken for the determination of the blood-sugar each half hour for three hours. The blood-sugar normally attains its maximum of 0.18 in half an hour, at the end of an hour has begun to fall and has returned to normal or even below by the end of the second hour. The fall in the blood-sugar is apparently due to the secretion of insulin by the pancreas, which can deal with the sugar as rapidly as it is absorbed, since the further ingestion of glucose has no effect. In diabetes this rapid fall is not seen, a high blood-sugar being maintained for some hours.

Hyperglycæmia or increased blood-sugar will also result from inability of the individual to use sugar, although the intake may be normal, a condition seen pathologically in diabetes mellitus, and which can be produced experimentally by stimulation of the splanchnic nerves, injection of adrenaline, stimulation of the floor of the fourth ventricle, and of the pituitary region.

The body uses sugar in three ways: it burns it as fuel, it builds it up into glycogen or animal starch in the liver and muscles as a store for immediate use, or it transforms it into fat in which form the energy occupies less space, although it is less easily available. Should the sugar intake be deficient these stores of energy are made use of. How this takes place and how increased requirement of muscular tissue brings about the discharge from the storage areas is by no means clear, although we know that both nervous and hormone stimulation may bring about excessive discharge from these areas and cause hyperglycæmia with glycosuria. Any stimulation of the sympathetic nervous system calculated to cause an outpouring of adrenaline from the suprarenal brings this about and the methods referred to above for producing glycosuria experimentally are of this nature. In the same way any emotion calculated to bring into action the emergency mechanisms has a similar result and the advantage in such circumstances of throwing into the circulation additional supplies of immediately utilizable fuel is obvious. It is considered by some that mental anxiety and strain may bring a similar sequence of events about in certain individuals. This is somewhat conjectural, as during war-time diabetes was not unduly common, but in this instance the effect of the anxiety may have been counteracted by dietetic reductions. It is also quite certain that this in no wise accounts for all cases of diabetes, as many most phlegmatic individuals are victims of the disease.

The work of Banting (1922) and those who followed in his wake has clearly demonstrated that the Islets of Langerhans in the pancreas are largely responsible for the proper utilization of sugar in the body, thus confirming the many pathological observations which demonstrated pancreatic disease in cases of diabetes. It had been shown in 1889 by von Mering and Minkowsky that removal of the pancreas brought about in animals a condition similar to diabetes in man and subsequently it was found that such a condition was not brought about by mere ligature of the pancreatic duct, although this procedure caused the secreting alveoli to degenerate.

The observations of Banting and his collaborator Best, founded as they were on the earlier purely scientific investigations, make a great modern romance and an excellent example of how investigation—vivisection, in fact—in the first instance purely for the sake of knowledge may be of enormous value to mankind.

Modern diagnosis of diabetes and treatment with insulin rest upon accurate determination of the blood-sugar. An increase of blood-sugar and glycosuria may also result from a variety of states although there is no actual disease of

the pancreas. It may be that the pancreatic secretion is inhibited or that actual secretion is prevented. But in each instance the emergency nature of the condition is evident. This is obvious in exophthalmic goitre, and carbon dioxide retention such as may occur in cardiac disease or interference with the respiratory tract, from tumour or injury to the brain, especially if interfering with the region of the pituitary or the floor of the fourth ventricle. It may also be noted during pregnancy and in a variety of temporary conditions such as epileptic convulsions, the paroxysms of malaria, the collapse of cholera, or injury to the liver, all of which are of interest not only to the clinician but in the more purely academic study of carbohydrate metabolism. The same may also be said of many of the signs and symptoms of diabetes mellitus. It is known quite definitely that pituitary extract and adrenaline antagonize the action of the extract of the Islets of Langerhans experimentally, and the glycosuria which results may be considered as a substantiation of the outpouring of adrenaline in emergencies. In the antagonism of pituitary extract will be explained the occasional glycosuria of pregnancy, as it is known that there is considerable increase of pituitary secretion in that condition.

PANCREATIC EFFICIENCY WITH SPECIAL REFERENCE TO DIABETES

It has long been known that disease of the pancreas was associated with the clinical condition of diabetes mellitus and that this condition could be simulated experimentally by extirpation of the pancreas from the animal. The essential feature of the condition is faulty utilization of carbohydrates which we now know depends on the inefficiency of the secretion of the Islets of Langerhans. Carbohydrates are absorbed from the intestine into the blood, but as they cannot be utilized the blood-sugar rises above the renal threshold and the excess of sugar passes out by the urine and is wasted. The excretion of sugar at the same time necessitates a considerable loss of water and polyuria results with the urine of high specific gravity. From the lack of carbohydrate fuel we have excessive appetite, and also as a result of the polyuria, excessive thirst. There is often a considerable feeling of weakness. The diagnosis when the symptoms are clear is confirmed by the finding of sugar in the urine, but absolute confirmation is obtained by determination of the blood-sugar and an indication of degree by the blood-sugar curve (see page 247). There is also a considerably diminished resistance to infection, and most cases of diabetes succumb eventually to intercurrent disease as the result. Often some minor symptoms of this nature, such as boils, carbuncles or pruritus, are the actual

complaint of the patient. Peripheral neuritis, the absence of reflexes and various other nervous and eye phenomena are common complications, but how these changes are brought about is not yet understood, but it seems likely that nervous tissue is particularly sensitive to inadequate metabolism and we know that lack of oxygen rapidly abolishes nervous function.

The most serious result of deficient carbohydrate metabolism is that the fats are insufficiently burnt, for, as we have seen, the fats burn in the fire of the carbohydrates. Normally the fats are oxidized for the most part, as shown by Dakin, by the process of beta-oxidation to CO_2 and water.* In this process the carbon atoms are oxidized two at a time and the fatty acid reduced to a lower member of the fatty acid series, a process made possible by the fact that all the natural fats contain an even number of carbon atoms. In passing through the stage of butyric acid, that is the four carbon atom stage, oxidation appears to be difficult, and if combustion is not sufficiently brisk from deficient carbohydrate metabolism, instead of the intermediate butyric acid being oxidized rapidly through to CO_2 and water, the intermediate products as the result of the slow reaction are found in such quantities that they may actually be excreted as such in the urine. These are β-hydroxy-butyric and aceto-acetic acids, from which latter acetone is formed by further oxidation. The formation of these two acids tends to deplete the alkali reserve of the blood and its carbon dioxide combining power and leads to a so-called acidosis or what is more explicit, as the acids are keto-acids, to a ketosis. Proteins may also contribute to their production. In addition, these substances are in themselves poisonous, and may account for some of the symptoms of the condition. There is, for example, excessive stimulation of the respiratory centre as the result of their existence, and the carbon dioxide in the alveolar air becomes appreciably reduced, a point often of value in confirming a diagnosis. If the state remains untreated, the accumulation of these abnormal substances finally overcomes the organism, and there results coma and death, if the patient has not died from intercurrent disease.

Treatment.—Knowledge of the physiological processes at fault at once indicates the treatment. In all modern treatment, in the severer cases at least, the administration of insulin overshadows all others. Insulin was so named by Sharpey-Schafer somewhat prophetically, as at the time the name was given, it was not absolutely proven that the Islets of Langerhans contained the

* More recent work by Raper and his co-workers indicates that beta-oxidation is not the only method by which fats are oxidized.

hormone responsible for efficient carbohydrate metabolism, although the evidence pointed in that direction.

Starting from the work of Banting, who showed by the use of extracts of fœtal pancreas in which the power to produce trypsin is not yet developed, and of organs of which the duct had been tied (to cause degeneration of the trypsin-producing cells of the gland), that trypsin destroys the insulin produced by the islets, Collip made use of the fact that the enzyme is inactive in alcoholic solution and prepared active alcoholic extracts of the gland with which dogs rendered diabetic by removal of the pancreas were successfully treated. It should be said that previous work, such as that of Zuelzer, had been attempted along these lines, but then apparently overdoses were used, as the blood-sugar level could not then be used as a control, and as the positive evidence, such as that of Banting, that the hormone was contained in the islets and was destroyed by trypsin, was not available, the experiments were not persisted in. Commercial insulin is made by improvements on the alcoholic extraction method. By its use many individuals have been rescued from coma which would otherwise have been fatal. Insulin is, therefore, a drug which should be in the possession of every practitioner, as a diabetic patient may often go into coma with dramatic suddenness. The insulin simply takes the place of the deficient internal secretion of the pancreas and renders adequate carbohydrate metabolism again possible. The treatment is as yet new, but there is now evidence that its continued administration allows the pancreatic islets to regenerate (Banting). The older methods of treatment calculated to rest the pancreas and to allow it to recover should therefore be continued.

A point which is worthy of notice in insulin therapy is the fact that excessive lowering of the blood-sugar may have dire results, as indicated above. Glucose should, therefore, be available for administration intravenously or by the mouth, according to the severity of the hypoglycæmia, which, however, is best prevented by the previous ingestion of carbohydrates.

Rest to the pancreas is accomplished by reduction of carbohydrate intake. Here it may be mentioned that it has long been a well-known clinical observation that diabetes not infrequently occurs in those who have been habitual overeaters. Allen has shown that the giving of large quantities of carbohydrate to dogs, rendered slightly diabetic by partial depancreatization, causes them to develop more severe diabetes. From this fact the value of keeping a mild diabetic on a low carbohydrate diet is evident and many so treated never develop severe diabetes. For general use the Allen treatment has been found very useful. The individual is made to starve for about a week, during which he

is kept warm in bed until sugar disappears from the urine. The carbohydrate tolerance of the patient is now estimated by the addition of known amounts of carbohydrate foods to the diet. As soon as the sugar appears again in the urine the amount of carbohydrate is noted and the fast resumed. When the urine is again free from sugar a quarter or half of the carbohydrate assimilation limit is given and the diet made up with protein and other articles which contain little or no carbohydrate. Gradually, by adding to the meat portion of the diet, which includes a small amount of carbohydrate and some fat, the diet gradually approaches the limit and if kept at this limit for a prolonged period it is found that the limit may slowly rise as the pancreas regenerates. At the same time general attention must be paid to the alimentary canal which may have contributed to the production of the pancreatic condition of a chronic inflammatory nature, as Cammidge has shown it does in a large number of cases. Details of treatment must be obtained from textbooks on therapeutics, but sufficient has been said to indicate the general physiological principles involved.

A word of warning is, however, necessary regarding the cutting off of carbohydrates suddenly, especially in fat diabetics. On starvation, the store of glycogen is, of course, first used up, but if the individual has a store of fat, this is now used, and its utilization may result in the flooding of the system with keto-acids, and coma may ensue. The carbohydrates, then, must not be taken away too quickly. It is not considered that such an occurrence is so apt to happen when the individual is thin, as there is little or no fat storage.

Once coma has developed little but insulin is of any avail. Patients have been kept alive temporarily by large doses of alkali injected intravenously, but obviously this is of no permanent value. The onset of coma, however, is reasonably preventable. Diacetic acid in the urine (aceto-acetic), which gives a red colour with ferric chloride, is always a danger sign, and when present alkalies should be given and the carbohydrates not unduly reduced.

CHAPTER XXX

THE FORMATION AND EXCRETION OF BILE

The comparatively crude fact that bile is composed of pigments formed from the destruction of effete red blood corpuscles and of cholesterol dissolved in a solution of bile salts has long been known, but of recent years a flood of new light has been thrown on the subject by clinical workers, especially McNee and van den Bergh. Many of our older conceptions of bile formation and of jaundice require revision, especially the location and method of the formation of bile pigments.

It seems now reasonably established that bilirubin is produced by the breakdown of the red blood corpuscles by the star-like cells of the reticulo-endothelial system which are found in the spleen, the bone marrow, and the venous capillaries of the liver where they are known as the von Kupffer cells. The best evidence that bile is not necessarily formed in the liver is that there is more in the splenic vein than in the splenic artery (van den Bergh), that the destruction of the liver in cases of poisoning (Dixon, Mann and Clegg) bears no relation to the amount of jaundice, and the occurrence of acholuric jaundice in which the removal of the spleen brings about recovery. This is supported by the finding of increased bile pigment in the blood in conditions of hæmorrhagic effusions and extravasations, while the colouring of a bruise has always been suspected as a process closely akin to the formation of bile.

The bilirubin when formed passes to the liver and is apparently modified in some way by the ordinary polygonal cells. This modification is made evident by the van den Bergh test, which is a modification of Ehrlich's dizao reaction in which sodium nitrite, specially prepared sulphanilic acid solution and ammonia are added to a sample of the blood serum and compared with reaction given by a solution of bile. The appearance of a pink colour given by bile is known as the direct reaction, but the appearance of the colour only after alcohol has been added is known as the indirect reaction, which is given by unmodified bile. By this test it is quite possible to determine bile in the blood both qualitatively and quantitatively by comparing with known standards. It is considered that not until the blood concentration of modified bilirubin has reached four

units does bile appear in the urine. [The arbitrary unit is one part of bile in 200,000 (Andrews).] The renal threshold for unmodified bilirubin is appreciably higher.

This conception of bile formation certainly affords an explanation for many of the known forms of jaundice and allied phenomena. The well-known discoloration in bruising has now been shown to be due to the formation of a true bile pigment and it has been shown that there is an increased quantity of unmodified bilirubin to be found in the blood when blood extravasations are being absorbed. The occurrence of slight jaundice under such conditions has often been noted. It has really been from a study of varieties of jaundice that our modern conception of the physiology of bile pigment formation has been drawn, thus emphasizing in modern times the necessity for scientific physiology to keep in contact with what appears to be purely medical research just as this correlation has proved necessary in the past in relation to work on the thyroid, pituitary and pancreas. The debt of physiology to the clinical observer becomes more obvious.

Jaundice may arise according to this conception in three different ways:

1. **Hæmolytic Jaundice.**—There may be an increased blood destruction to an extent which the polygonal cells of the liver cannot deal with, as the pigment is so rapidly produced. In this category will come these forms of jaundice which used to be called hæmatogenous, of which the anæmias, especially pernicious anæmia, and cases of absorption of hæmorrhagic effusions, are examples. Such forms are now more accurately known as hæmolytic jaundice. As the bile pigment forms in excess and has not been modified by the liver, the blood serum will give an indirect van den Bergh reaction.

2. **Toxic or Infective Jaundice.**—Here the blood pigment may be normally produced but, as the result of the impairment of the liver, it may not be drained off sufficiently rapidly. The unmodified pigment will accumulate in the blood and give a marked indirect van den Bergh reaction. The impairment may occur to any degree and thus the test may be of little value in distinguishing between this type and the hæmolytic variety, although where the liver is diseased the reaction appears to be more marked. It will be obvious, too, that should the impairment not be severe, or be local, some of the pigment may become modified, but owing to the state of the liver, and its passages, it may not be adequately excreted and on being reabsorbed cause a direct reaction. Ordinary catarrhal jaundice appears to be of this variety. There may be an intense indirect reaction from liver impairment, probably hepatitis, especially at first. Later on, possibly from obstruction by disintegrated corpuscle or

cholangitis, there is reabsorption of fully formed pigment and an indirect reaction is obtained as well as a direct one. This supports other evidence, e.g. the lævulose test (page 344), which indicates that catarrhal jaundice has a very definite hepatic origin.

3. **Obstructive Jaundice.**—Here the bile pigment is normal in quantity and quality, but cannot escape from the liver and reabsorption occurs from the bile capillaries. Such a condition will occur in simple obstructive cases, due, for example, to gallstones impacted in the common duct, cancer of the head of the pancreas, or new growths otherwise present on the bile duct, and the van den Bergh reaction will be direct as the bile passes through the liver in the normal way. It will be obvious, however, on general principles, that an increase in the pressure of the bile capillaries must lead to an impairment of the capacity of the polygonal cells to modify the bile. Hence the blood serum may show an accumulation of unmodified bile giving an indirect action. The pink colour produced in the direct reaction will be enhanced by the addition of alcohol, the whole reaction being then, as it were, diphasic.

It will be evident that in diagnosis the van den Bergh reaction must be interpreted with due regard to the state of the patient and the duration of the complaint.

Of special interest is the fact that the reaction has brought to light instances in which the patient, in virtue of a high amount of unmodified bilirubin in the blood, may be assumed to have what may be called a *latent jaundice*, which will become evident if the liver becomes further impaired, e.g. by salvarsan treatment. The fact that glucose (Harrison) has been found of value in preventing jaundice after salvarsan suggests that the glucose must play a part in the normal modification of bilirubin in the liver, just as does the alcohol if added to the unmodified bilirubin in vitro. The close relationship of glucose to alcohol chemically appears to favour this possibility.

Quite apart from the jaundice produced, the retention of bile will tend to bring about a characteristic pale and fatty stool of steatorrhœa, since we know that the bile salts play an important part in facilitating, by co-operation with the pancreatic juice, the digestion and absorption of fats. The colour of the stools is, then, of importance as is also the content of fat in arriving at a conclusion regarding the cause of jaundice.

The bile salts have also an important function in keeping in solution cholesterol which is derived from the breakdown of red blood corpuscles and nervous tissue. Normally this solution is complete, but under certain circumstances such as excessive production of cholesterol, or as a result of the addition of

bacterial products, the cholesterol may become precipitated and give rise to gallstones.

Of considerable clinical importance, also, is the fact first noted by Meltzer that magnesium sulphate applied to the duodenum in the region of the ampulla of Vater causes the relaxation of the sphincter of Odi and gall bladder to contract and drive out bile, while use has been made of this by Lyon in investigating the biliary tract by means of the Einhorn tube passed into the duodenum (see also page 225). It is considered that three distinct fractions of bile can be obtained, one a golden brown derived from the bile duct, the second from the gall bladder, and the third from the liver, which may be studied bacteriologically if necessary. In ordinary practice the administration of magnesium sulphate results in very bile-stained stools, the occurrence of which may be considered good evidence of the patency of the bile duct.

For the tests for liver function the reader is referred to the excellent manual of Beaumont and Dodds.

CHAPTER XXXI

THE URINE

The importance of the examination of the urine in almost every case of disease has been impressed upon a generation of medical students. While physiology continues to emphasize its value in diagnosis, one must bear in mind the too-often overlooked fact, even in more scientific circles, that the kidney is only part of the general excretory system, and that the large intestines and skin may be quite as important.

For many years the pure physiology of the urinary system has been dominated by arguments for, and against, the various theories of urine production. To clinical observers there is another aspect which is more important, namely, the effect which deficient kidney excretion may have on the body, and the prospects of treatment and recovery.

Anatomy.—A few anatomical details of the structure of the kidney should be kept in mind. The starting-point of urine formation is the glomeruli—bunches of capillaries hanging down into the capsules of Bowman which is really the dilated beginning of a urinary tubule. The glomeruli are more concentrated in the region of the cortex. Each capsule becomes continuous with a uriniferous tubule. These tubules in different parts exhibit varying features, in one part being straight and lined with a flat epithelium, in another being convoluted and lined by cells suggestive of active function. Briefly stated, the position regarding kidney secretion is as follows: It is admitted that the fluid part of the urine is for the most part excreted by the glomeruli, probably by a process very analogous to filtration. But the difficulty is in regard to the solids. There are two main divisions of opinion in this matter, one (Ludwig, Cushny) that the urine with the solids in very dilute solution is secreted by the glomeruli and that the urine is subsequently concentrated during its passage down the tubules; and secondly (Bowman, Heidenhain), that only water is excreted by the glomeruli and that the solids are added to the urine in its passage down the tubules. That both processes in the modern forms of these views require the assistance of some vital action on the part of the tubule is generally admitted, as it can be demonstrated that oxygen is required in proportion to the activity. There is, perhaps, a weight of opinion in favour of

the reabsorption theory championed by Cushny, largely because many of the pathological findings can be explained by it. There are, however, many facts which it does not explain, and we as yet see very dimly. To one who studies the evidence impartially it does not seem impossible that the truth may lie between the two opposing views, for each is not exclusive of the other, as at first sight might appear. We know, for example, in disease of the kidney that certain substances normally excreted are retained. But the retention of different substances, such as urea and creatinine, bears no constant relation to each other nor to the extent to which they are concentrated from the blood in the urine. These are facts which appear to indicate that different parts of the kidney mechanism have different and selective functions in the excretion of solids. This is supported by the observation that certain of the urinary contents are influenced by the injection of various hormones, while others may be unaffected.

The functions of the kidney are to excrete water, to excrete unrequired salts and products of metabolism, especially protein metabolism, to assist in maintaining (by varying the excretion of phosphate and ammonia) the neutrality of the blood, and to eliminate toxic substances and bacteria. Examination of the urine, then, can give a considerable amount of general information regarding the body as well as local information regarding the kidney. These are best described under the several characteristics of the urine.

Quantity and Specific Gravity of the Urine.—Normally an individual leading an average life should pass about 50 ounces daily or 1.5 litres, but as shown in more detail, in relation to the water content of the body, the actual amount will depend very much on how much water is lost in other ways, e.g. by the skin, by the respiration, or by the intestine. Here it should be said that it is often impossible to take the word of a patient in relation to polyuria, as not uncommonly frequency of micturition is confused with polyuria, in which the quantity is increased. Attempts have been made to use the quantity of the urine excreted in a given time after a given intake as an index of kidney efficiency, but this is found most unsatisfactory because of the individual variation. Those who habitually consume large quantities of fluid may, by this test, appear to have very efficient kidneys, although a large part may be out of action.

The amount is increased if the body requires to get rid of any soluble substance. Thus we see sulphates have a diuretic action, as has sugar in diabetes. In the polyuria of chronic nephritis, on the other hand, we must consider that the urea which is in excess in the blood has a direct stimulating action on the

kidney cells, and we know that in experimental urea diuresis additional oxygen is consumed by the kidney. The excessive excretion of urine is not then necessarily due to the usually accompanying high blood pressure, as has been suggested, although no doubt this assists. More urine is excreted by day than by night, but as the total amount of solid does not vary so much, night urine is appreciably more concentrated than day urine. The normal specific gravity varies from 1.015 to 1.025. In chronic nephritis, under the stimulation of the increased urea in the blood, the diminution of night volume is not seen and the specific gravity remains below normal throughout.

The association between the solids to be excreted and the amount of urine passed is also seen in diabetes insipidus, where the polyuria may be the only symptom. There is no excess of sugar. The injection of pituitary extract acts as a charm in causing the amount secreted to return to normal. The recent experiments of Starling and Verney suggest that the posterior lobe of the pituitary controls the facility with which the kidney can excrete chlorides. In diabetes insipidus this appears to be reduced, and, as we shall see in the case of difficulty in excreting urea, more water has to be got rid of in order to obtain the same total excretion of chlorides per day, otherwise they would increase progressively in the blood. Until we are clear as to the exact mechanism of urine secretion it is difficult to go further than this, but that the pituitary body has a definite action in this respect is seen clinically in conditions of intra-cranial tumour or injury to the gland. The polyuria of chronic interstitial nephritis is brought about in a similar way by local conditions interfering with the urea excretion.

A reduction in the amount of urine secreted will be brought about by diminished intake of fluid, or, if there is excessive loss, by the bowels or skin. This is dealt with more fully in Chapter XXXIII. Anuria may result from local obstructive conditions, such as blockage of the ureter, and is a very serious condition. It may, however, result from increased tension in the kidney from acute inflammatory causes, for the capsule of the kidney is inelastic, like the pericardium, and any increased tension must result in compression. Various attempts have been made to relieve such tension by stripping the capsule. This operation cannot be expected to do good where there is no increased pressure, as in the more chronic conditions. There is evidence suggesting that any improvement which results may also, in part, be due to reduction of the channel of infection which apparently may be by way of the lymphatics and the capsule.

Similarly, there is anuria if the kidney is destroyed by poisons, such as lead

or phosphorus. Of considerable interest, too, is hysterical anuria which emphasizes the nervous control of the kidney, presumably that of its blood-vessels.

The Reaction of the Urine.—The reaction of the urine in man is, when passed, distinctly acid as the result of a preponderance of faintly acid salts, chiefly the acid phosphates. In this connection it is well for those not acquainted with the subject to read Chapter XXXII at this point, where the significance of the balance between the alkaline and acid phosphates is discussed. It will there be seen that wherever the body requires to neutralize acid an additional amount of acid phosphate is excreted, the alkali being available from the alkaline phosphates. On the other hand, if respiration has been stimulated by any means other than by carbon dioxide, an excessive amount of this gas is washed out of the lungs and the acid phosphate is retained in the body to the extent of the alkaline salt. That the two salts are interchangeable readily is seen by the formulæ and the following reaction:

$$Na_2HPO_4 + HCl = NaH_2PO_4 + NaCl$$

alkaline phosphate + acid = acid phosphate + neutral salt,

or, what is more usual physiologically:

$$Na_2PO_4 + H_2CO_3 = NaHPO_4 + NaHCO_3$$

alkaline phosphate + carbonic acid = acid phosphate + sodium bicarbonate.

The alkaline salt acts as a store of alkali and the acid salt as a store of acid, which is of value in maintaining the neutrality of the blood. There is also a change in some of the other salts excreted, e.g. ammonium salts and urea, but the reaction of the urine is not affected by these.

Use has been made of the determination of the reaction of the urine in the investigation of *acidosis*. The determination of the hydrogen ion concentration is now of recognized value. This may be done directly by means of the use of some of the newer indicators or an estimation may be made of the amount of alkali which has to be added to render the urine neutral. It has been found by Van Slyke, the well-known authority on the subject, that when the urine excreted is neutral to phenolphthalein the carbon dioxide combining power of the blood (see Appendix) is maximal. If this power is reduced the urine will be correspondingly acid.

The determination of the amount of sodium bicarbonate which has to be administered to an individual to change the reaction of the urine is recommended by L. J. Henderson and Palmer. It is considered by many who have experience of it, to be the best method of ascertaining the presence and degree of

acidosis. A series of colour standards which correspond to a given hydrogen ion concentration and the required indicator are easily procured. In a normal individual five grammes of bicarbonate of soda will suffice to lower appreciably the hydrogen ion concentration of the urine. This test of Sellard is, however, according to Maclean, of no value as an index of acidosis in nephritis, for the defective kidney fails to eliminate the alkali.

Leathes has shown that in the forenoon the respiratory centre is more active than at other times, and an excessive amount of carbon dioxide is got rid of. Less acid is therefore excreted by the kidneys and the urine becomes alkaline. Forced breathing will also bring about a similar result. He suggests that changes in this alkaline tide might be utilized as an indication of the alkaline reserve of the blood.

In the above tests the urine must be freshly voided, and not allowed to stand, for the urea is so easily broken down by bacterial fermentation. Camphor or toluene may be used as preservatives. Thymol is not so satisfactory as used to be thought. The same will apply to cases where there is infection of the urinary tract or undue retention. An alkaline urine will usually result from a herbivorous diet, because of the carbonates which result from the breakdown of the organic acids present. This should be borne in mind, for phosphates may be precipitated, giving a milky appearance to the urine which may cause alarm.

On the other hand, an unduly acid urine may result from excessive meat eating, from certain fruits (prunes and cranberries) which contain benzoic acid, and even cereals which contain much protein—whole wheat or rice. In diseases where there is a great breakdown of protein, the acidity of the urine is increased. This is still further the case when abnormal mineral acids are produced, e.g. dihydroxybutyric in diabetes. Excessive exercise will lead to the production of a urine of increased acidity because of the increased production of carbon dioxide.

THE CONSTITUENTS OF THE URINE

Of recent years a great deal of attention has been paid to the significance of the constituents of the urine in health and disease, as it is found that some of these may not only be an index of the functional efficiency of the kidney but also of a large variety of conditions which may influence the neutrality of the body. It is convenient to consider several of the more important constituents, one by one.

Urea.—This is undoubtedly the most important urinary constituent. Indeed, there is evidence that urea may be considered the normal stimulant of the kidney just as carbon dioxide is of the respiratory centre. Urea is, as we have seen, derived from the breakdown of protein by the conversion of the amino portion of the amino-acids into ammonia, and its subsequent linking up with carbon dioxide to form ammonium carbonate and later urea. It must depend, obviously, to a large extent, on the amount of protein in the diet. In an individual on an average diet urea is found in the blood to the extent of 20 to 40 milligrams per 100 c.c. of blood or 0.02 per cent. to 0.04 per cent., the upper limit being reached in older people, in whom it is not infrequent to find the higher figure exceeded. The daily excretion of urea in the urine amounts to 30–40 grammes. It appears that in some normal individuals, but especially those with chronic interstitial nephritis, a high concentration or "head" of urea is necessary before the daily amount of urea can be got rid of. As emphasized by Maclean, this cannot be appreciably reduced, otherwise the individual would soon became saturated with urea. The blood urea is, therefore, not an index of the efficiency of the kidney except where there has been gross impairment. Animal experiments suggest that the organ may be destroyed to the extent of three-quarters before there is an actual accumulation of urea. This, however, may occur in more acute varieties of nephritis. According to Maclean, whatever the clinical condition of the patient, even when he is apparently improving, so far as his general condition and œdema are concerned, a rising blood urea indicates that a fatal termination is not far distant, while on the other hand, however severe the symptoms, a falling blood urea indicates a good recovery. Special warning is given regarding the value of blood urea estimations in cardiac and infected conditions in which the blood urea is apparently high simply because the blood does not pass through the kidneys sufficiently often. To be of value blood urea has, then, to be considered with other evidence of kidney efficiency.

The mere estimation of urea in urine is, unfortunately, not of the same value, for the percentage is so liable to be affected by a large number of conditions, such as those affecting body neutrality, diet, and the like. By the method of Maclean and de Wesselow, the patient, after emptying his bladder, is given a quantity of urea (15 grains) in a small quantity of water (100 c.c.). Specimens are taken, one and two hours afterwards, and if the kidney is efficient these should contain above 2 per cent. of urea. Occasionally the test is interfered with by excessive diuresis (over 120 c.c. in the second hour), and hence the second specimen rather than the first is more trustworthy. A third may

even be necessary and even to restrict the fluid intake prior to the test. It has been found that the *power of the kidney to concentrate urea* is reduced in nephritis long before the blood urea rises, as indicated above. The factor obtained, however, by dividing the concentration of the urea in the urine by that in the blood is also some indication of the urea-concentrating power of the kidney. This is normally about 90, but in severe nephritis may be reduced below 10. This test obviously requires more time than that just mentioned.

Ammonia.—This is derived from the same source as the urea, namely, the de-amination of the unrequired amino-acids which result from protein digestion. Small quantities may be taken as such in the food or may be produced by bacterial action. Normally, as we have seen, the ammonium carbonate which is formed by combination of carbon dioxide is converted into urea chiefly by the liver. The daily excretion is 0.6–0.7 gramme.

The ammonia plays an important part as a source of alkali in the body, as it is used to neutralize acid radicals which may be excreted as ammonium salts, the amount of urea being correspondingly reduced. There is evidence that in this neutralization the kidney plays an important part by breaking down the urea again and reforming the ammonia. It has been found, for example, by Nash and Benedict that if the kidneys are removed there is diminution in the ammonia in the blood, and that normally the concentration of ammonia is greater in the renal vein than elsewhere. Although urine ammonia is increased by the injection of acid, this is not so with the ammonia in the blood, as might at first sight be expected. It has also been found by Maclean that in conditions of acidosis, due to kidney disease, the increased ammonia excretion found in other forms of acidosis is not seen.

The ammonia-urea ratio (normally 1 to 50) is a usual method of following changes affecting body neutrality. Alternatively the ammonia nitrogen may be expressed as a percentage of the total nitrogen. This is normally about 5 per cent., but pathologically in acidosis may reach 20 per cent. Throughout the above remarks it is to be understood that what has been said refers to urine freshly secreted, as on standing it is readily broken down by the bacillus ureæ with the formation of ammonia.

Creatinine.—The constancy of the amount of creatinine (1 to 2 grammes per day) excreted normally is as striking as the variability of the urea content. As shown by Folin, variations in diet make practically no difference in the amount. It is thus quite clearly a product of endogenous metabolism, and is found approximately in proportion to the total muscle in the body. The exact origin of this substance is not quite clear, but its excretion is definitely increased

when the individual is breaking down tissue, as in starvation or the involution of the uterus. The constancy with which it is produced has caused its excretion to be used as a test of renal efficiency. It is generally accepted that a high blood creatinine (over 5 milligrams per 100 c.c. as compared with 1 to 2 milligrams) is of very grave significance in kidney disease. Apparently, it is not until the kidney is much diseased that there is any appreciable creatinine retention.

Uric Acid.—This is derived from the nucleo-proteins of the diet, especially, from tissues rich in nuclei, such as liver and sweetbread. It may appear as a "cayenne pepper" deposit in urine, but usually it is combined with alkalies to form urates which, when concentrated, fall out of solution and cause the typical brick-dust deposit on standing, especially in an acid urine.

Phosphates.—These, we have seen, play a special rôle in relation to the maintenance of body neutrality. The acid hydrogen phosphate, NaH_2PO_4, is chiefly responsible for the normal acid reaction of the urine, since normally the acid products in an average meat diet preponderate. If, on the other hand, a vegetable diet is taken, it is necessary to get rid of alkali excess, which is done by increasing the amount of alkaline phosphate excreted (Na_2HPO_4). The following reaction indicates how the alkali is available for the neutralization of acid, $Na_2HPO_4 + CO_2 + H_2O = NaH_2PO_4 + NaHCO_3$. The acid phosphate and the sodium chloride are excreted. The phosphates are commonly excreted as sodium, potassium, or calcium salts, but in a fermented urine the triple phosphates NH_4, Mg, PO_4 (ammonia-magnesium phosphate) appear. The latter are commonly seen as crystals of the typical coffin-lid type and when they occur in freshly voided urine are considered to indicate the presence of infection in the urinary tract which facilitates ammoniacal fermentation. In a stale urine, in which the ammoniacal fermentation has taken place outside the body, the presence of such crystals is of no significance.

Clinically, the passage of a milky urine is often found when the urine is alkaline and if phosphates excreted for reasons given above are excessive. This can easily be remedied by increasing the protein intake. It is suggested that phosphates are also derived from the phosphorus-containing articles of the diet, such as the nucleo-proteins, lecithins, and the like. Phosphaturia may indicate excessive waste of nervous tissue, as in excessive mental work, wasting diseases and the like, and there seems to be little doubt that in some individuals such conditions bring about an increase in the phosphorus excreted. The actual variety of phosphate will depend, in the absence of disease affecting the excretion, on the variety of the diet and the amount of exercise taken, as the latter

produces carbon dioxide and lactic acid and thereby brings about the excretion of the acid variety.

Occasionally alkaline phosphates are just kept in solution by the amount of carbon dioxide which is dissolved in the urine. On heating this is driven off and the phosphates are precipitated. This opalescence may be confused with that due to albumin and hence the necessity of faintly acidifying the urine (best with acetic acid) before so testing.

Oxalates.—These have a special significance in that some individuals appear to be unable to break up oxalates normally. Such substances occur in tomatoes, rhubarb, strawberries, cabbages, spinach and asparagus. A little occurs in apples and grapes. Apparently all the oxalates of the urine do not come from the food, as a dog fed on meat and fat excretes oxalates (Mills). Experimental and chemical evidence suggests that oxaluria may be brought about by abnormal oxidation of uric acid. The urine standing is described as having a "powdered wig deposit" on the top of the mucus or any other deposit present. If concentrated, it may give rise to disagreeable symptoms of irritation during micturition. So sensitive are some individuals that they may be affected by a single strawberry. Treatment is obviously directed to elimination of oxalates from the diet and the administration of diluents.

Excretion of Dyes.—Although, as yet, we are somewhat in the dark regarding the exact mechanism of the excretion of dyes, there seems to be little doubt from clinical evidence that the facility with which the kidney can excrete these substances is a measure of its efficiency as an organ of excretion. Dyes such as indigo-carmine or methylene blue are often sufficient to give an indication of the relative amount of excretion by each kidney. The outpouring of the dye in spurts from the ureters may readily be observed by the use of the cystoscope, but for more accurate work catheterization of the ureter is desirable and the amount of dye excreted by each kidney estimated. The phenolsulphonephthalein test of Rowntree and Gerraghty has received most attention in this connection. In carrying out the test the dye is injected into the buttocks of the patient, and estimation of the amount passed after one hour and after two hours is then made by comparing the urine colorimetrically with a standard solution. It is considered that 70 per cent. of the pigment should be excreted in the second hour. If only 50 per cent., recovery is to be expected under treatment, while below 20 per cent. prognosis is bad, and if this low value persists death is not far distant.

Diastase.—Normally, the diastase used for the conversion of starch and glycogen into sugar is excreted by the kidney and in different individuals the

daily excretion is very constant. The measurement of the excretion is very easy, the standard being the amount of dextrin which is converted into glucose in a given time. Normally, this is 6 to 20 units, but in disease it may be under 1. Fallacies will apparently be very common, as it might be considered that in diabetes, for example, the diastase would be appreciably reduced, but it has been pointed out by Cammidge, Forsyth and Howard that the diastase in the blood is not appreciably dependent on the pancreatic diastase and its reabsorption, but is produced by the liver, since it is shown that excision of the pancreas tends to cause the blood diastase to be increased, whereas destruction of the liver brings about reduction. Liver disease, as found by Harrison and Lawrence, also reduces appreciably the blood diastase which apparently is that elaborated by the liver for the conversion of glycogen into glucose. The value of glucose injections in protecting against the effect of salvarsan is considered to be due to the fact that in some circumstances the liver may be unable to produce an adequate amount of glucose in the normal manner. It will be evident from the above that the estimation of the diastase excretion, although it may be of supplementary value, does not necessarily give much information regarding the kidney.

CHAPTER XXXII

THE MAINTENANCE OF BODY NEUTRALITY

Under normal conditions the body is constantly being subjected to states which tend to alter the reaction, or hydrogen ion concentration, of its fluids. Those who are not familiar with the term hydrogen ion concentration of the blood and the mechanism by which the gases are carried by the blood are advised to read the Appendices on these subjects (page 343).

The food ingested may be acid or alkaline or may be made so as the result of digestion and metabolism. In exercise large amounts of carbonic and lactic acids are produced, while in digestion alkali and acids are poured out. Tissues are very sensitive to change of reaction. A very small increase is incompatible with life, although apparently alteration to the alkaline side is the more easily tolerated. A general idea of the neutrality of the body is furnished by the blood which keeps the different parts at equal hydrogen ion concentration. According to Sörensen's nomenclature, neutrality is expressed by pH 7.0 for reasons explained on page 349. In this nomenclature the reaction of the blood is 7.4, which is just on the alkaline side. Life is possible between pH 7.2 and 9.0, although such variations have never actually been demonstrated in man. This range is extremely small and a number of factors combine to maintain the reaction in the neighbourhood of 7.4. These are: the blood salts, the respiration, the liver, the kidney, and the intestines. All these factors are interdependent, so that if one fails more strain is thrown on the remainder. Further, when it is considered that the normal hydrogen ion concentration of the blood is equivalent to 1 gramme of hydrogen in 32 million litres of water, it will be realized how extremely delicate these vital mechanisms are. No scientific apparatus yet designed has approached anywhere near their sensitivity.

The Blood.—The addition of acid or alkali makes little or no difference to the reaction of the blood. This is because of its "buffer" salts which, as it were, soak up (the original word used by Fernbach and Hubert was *tampon*, and translated into German, "Puffer") the hydrogen or hydroxyl ions which are excreted by the lungs and kidney in a less active form. The buffer salts are sodium bicarbonate ($NaHCO_3$) and alkaline sodium phosphate (Na_2HPO_4).

Suppose, for example, hydrochloric acid is added to the blood: then we have interactions—

(1) $NaHCO_3 + HCl = NaCl + H_2O + CO_2$ and
(2) $Na_2HPO_4 + HCl = NaH_2PO_4 + NaCl.$

In each instance we have a salt formed and a weak acid or an acid salt. It will further be seen that the carbon dioxide can react with the phosphate, and supply more bicarbonate, thus—

$$Na_2HPO_4 + CO_2 + H_2O = NaH_2PO_4 + NaHCO_3$$

As the chief store of alkaline phosphate is in the red blood corpuscles, the reaction takes place in two stages, thus—

$$CO_2 + H_2O + NaCl = NaHCO_3 + HCl.$$

The acid passes at once into the corpuscles to reform potassium chloride according to the equation,

$$NaHKPO + HCl = KCl + NaH_2PO_4.$$

The phosphates, although playing an important part in buffering, do not leave the corpuscles unless in excess.

The same reactions will occur when carbon dioxide is added to the blood by muscle activity. The importance of this reaction in the body, when there are conditions which tend towards an accumulation of carbon dioxide, is evident. Further, if carbon dioxide is added in the body, sodium bicarbonate is formed at the expense of sodium chloride of the plasma, the hydrochloric acid entering the corpuscles and combining with the phosphates, as shown above. It also combines with the alkali set free by the oxyhæmoglobin when the latter becomes reduced to hæmoglobin in the tissues. (See also the Appendix on the "Respiratory Function of the Blood.") A small amount is carried as acid in solution. This is balanced by the amount of the (alkaline) bicarbonate in the blood. We may consider the reaction of the blood to be proportional to

$$\frac{H_2CO_3 \text{ (carbonic acid)}}{NaHCO_3 \text{ (sodium bicarbonate)}}.$$

Actually, the venous blood contains 60 c.c. of carbon dioxide, of which about 3 c.c. is in solution. The ratio is then, normally, one-twentieth.

The reaction of the blood will then be changed by adding carbonic acid or removing bicarbonate. The former is brought about by exercise, the latter by the addition of acids, such as lactic acid in exercise and β-hydroxy-butyric in diabetes. In both instances, provided the addition is not excessive, the balance is maintained by the excretion of carbon dioxide from the lungs in proportion. For example, if bicarbonate is reduced, an additional amount of carbon dioxide

has to be got rid of to maintain the normal ratio. This is brought about automatically by the response of the respiratory centre. For most purposes, then, the essential factor in the maintenance of the neutrality of the blood is a store of alkali or what is now commonly called the *alkali reserve*. In practice this is taken to be the carbon dioxide fixing power of the blood under certain conditions. In the first instance, alkali for the formation of bicarbonate is set free by the reduction of the oxyhæmoglobin to hæmoglobin, more is set free by the phosphates and in emergency the tissue cells and tissue fluids (Henderson and Haggard), and, according to some authorities, protein may be called into use to take up acid.

At first sight, if conditions in the body are considered to be identical with those which can be reproduced in a test-tube, it might be considered that a diminution in the alkali reserve of the blood necessarily indicated the addition of an abnormal acid to the blood. As has been emphasized by Haldane and by Yandell Henderson, a compensatory fall in the alkali reserve may also occur in an alkalosis. Thus, if for any reason, such as excessive sensory stimulation or oxygen want, the sensitivity of the respiratory centre be increased, an excessive amount of carbon dioxide may be lost. Under such circumstances there is a compensatory reduction of the blood alkali which may readily be mistaken for an acidosis, when in reality it indicates an alkalosis. Usually the urine will show the exact nature of the case.

Liver and Kidney.—These organs play an important part in the neutrality of the blood. The kidney is of particular importance in the excretion of acid. We have seen that if acid is added to the blood the alkaline phosphate is converted into acid phosphate, thereby releasing alkali. This acid phosphate is got rid of by the kidney and indeed this is the normal process. The acid phosphate is the chief acid constituent of the urine. Should, on the other hand, there be excessive acid loss, as, for example, when the respiratory centre has been over-stimulated and carbon dioxide is washed out of the lung, then little or no acid phosphate will be found in the urine and excessive phosphate, if there is any, is got rid of as an alkaline salt, which causes the urine to be alkaline. It is obvious, then, that should the kidney be diseased, there will be a retention of the normal excretion of acid phosphate, as is seen in nephritic. Owing to the accumulation of acid, respiration is stimulated to get rid of it as carbon dioxide. This is an important factor in the production of the typical dyspnœa seen in uræmia. The acids take up some of the available alkali, and the carbon dioxide combining power of the blood may be markedly reduced. This we know as a diminution in the alkali reserve or acidosis, as it is com-

monly called. It must, however, be admitted that much of the clinical evidence on this point is unconvincing.

The liver is the main organ responsible for the production of urea. By the de-amination of the amino-acids resulting from protein digestion, large amounts of ammonia are produced. Some of this is converted into urea, some unites with the acids and is excreted as ammonium salts. Thus the more the ammonia required to combine with salt, the less will be the urea secretion, and *vice versa*. How and where the actual process takes place is by no means clear. There is evidence which suggests that urea may be first formed, and that the kidneys subsequently break it down again into ammonia if this is necessary (see page 263). Probably also some of the ammonia unites directly with acids as it is formed in the de-amination. It is quite clear that ammonia is made use of to get rid of acids. For example, if the breath is held or in asphyxial conditions, an increase of ammonium salts in the urine may be readily demonstrated, while after a period of forced breathing there is a corresponding reduction in the excretion of ammonium salts. This has been dealt with already in relation to the urine.

Respiration.—This has already been considered, but from what has just been written it is evident that it is also of first importance in the maintenance of the normal reaction of the body and of the ratio

$$\frac{H_2CO_3 \text{ (carbonic acid)}}{NaHCO_3 \text{ (sodium bicarbonate)}} = 1/20.$$

The slightest increase of numerator (or a decrease in the denominator) will increase this ratio. Such a state of affairs will tend to occur if an acid is added to the blood, carbonic acid being set free in solution in the plasma, as indicated in the equations given above. This carbon dioxide will stimulate the respiratory centre, and the increased breathing will bring the ratio to normal. Thus we see the important part respiration plays in the excretion of the excess of acid. Should the respiratory centre be capable of responding sufficiently to accomplish this, the condition is known as a *compensated* acidosis. If not, and if the ratio is permanently increased, the condition is considered an *uncompensated* acidosis. Similarly, the respiratory mechanism is of importance in the retention of acid when this is necessary. This is dealt with further in relation to the significance of alveolar carbon dioxide.

The Intestines.—Apart from the fact that alkaline phosphates are excreted by the intestines, we have little accurate information regarding this excretion. It is, however, a well-authenticated fact that a sharp purgative is frequently

of value in a threatened acidosis. How the improvement is brought about is not clear, but in some way the excretion of acid products is facilitated.

ALVEOLAR CARBON DIOXIDE AND ITS SIGNIFICANCE

The comparative ease with which an analysis of carbon dioxide and oxygen in alveolar air may be made and the fact that normally there is almost equilibrium between the blood and alveolar air suggests at first sight that analysis of the alveolar air would be a very valuable index of the carbon dioxide in the blood and be of use in diagnosis. The principle of the method is to obtain a sample of the air breathed out at the end of a deep expiration. This may be done by Haldane's method, in which the patient expires deeply through a tube which is provided at its proximal end with a T-piece through which the sample can be withdrawn. Dodds has introduced the simple and apparently reasonably reliable method of asking the patient to whistle rapidly through the lips and when the note begins to fall off, the nozzle of a 10 c.c. syringe is pushed into the aperture between the lips and a sample of the air in the mouth collected. In each instance the sample is rapidly transferred to a gas analysis apparatus in which the carbon dioxide is measured by determining the diminution in a measured volume which occurs on exposure to sodium hydroxide. Unfortunately the method is not nearly so valuable as might be expected because individual cases differ so much. It might be expected, for example, that a fall of carbon dioxide results from the excessive breathing in consequence of stimulation of the respiratory centre by abnormal acids, and that the method would be a means of diagnosing the presence of such acids in the blood. Unfortunately, breathing is stimulated by so many other things which not infrequently complicate conditions in which there are abnormal acids which influence the respiratory centre that alveolar carbon dioxide can only be of confirmatory value in diagnosis.

A broad generalization can, however, be made regarding changes in the alveolar carbon dioxide.

A rise in this gas occurs whenever there is an increase of it in the blood without any other complication and provided it can reach the alveoli from which the sample is taken. Normally we consider this to occur in exercise. It is also increased when there has been an excretion of acids (Dodds), e.g. hydrochloric acid, in the early part of digestion. Respiration is then depressed as the result of removal of acid and carbon dioxide is allowed to accumulate in the blood and alveoli in order to keep up the hydrogen ion concentration of the blood to normal. The presence or absence of this temporary rise of

alveolar carbon dioxide may be taken as indicating under- or over-secretion of gastric hydrochloric acid. In cases of hypersecretion the alveolar CO_2 has been found to be as high as 15 per cent. (Dodds). A similar rise of carbon dioxide in alveolar air will result if quantities of bicarbonate are taken (Haldane), as the gas has to be retained to maintain the ratio $\frac{H_2CO_3}{NaHCO_3}$ normal.

There will also be a rise where there has been faulty replacement of alveolar air from one of several causes (see page 151). The existence of such a rise, however, will be obvious without actual analysis being made and, indeed, in such circumstances, it may be difficult to get a sample.

A fall in alveolar carbon dioxide results whenever the respiratory centre is stimulated other than by increased carbon dioxide production. This stimulation is of two main types, one of which is an acidosis, in which the chemical state of the blood is the cause of the abnormal respiration, and the other in which there is an alkalosis where the blood condition is secondary to the changes in the respiration.

The first state occurs when abnormal acids exist in the blood, as in diabetes and uræmia, and the second may be due to a great variety of conditions. In the latter category are conditions in which the sensitivity of the respiratory centre to the normal carbon dioxide of the blood is increased, as in oxygen want, and as is common in excitement or sensory stimulation of various kinds. In these cases the carbon dioxide has been washed out of the body as the result of the excessive action of the respiratory centre, and an alkalosis, with diminished hydrogen ion concentration of the blood, is produced.

From a study of the mechanism for the maintenance of body neutrality it will be evident that the two classes are similar only so far as the carbon dioxide in the alveolar air is concerned. In the case of the addition of abnormal acids the body attempts to get rid of the acid by the urine which is characterized by being acid, with a diminished urea content and increased ammonium salts. On the other hand, in the case of increased sensitivity of the respiratory centre or of nervous stimulation, the opposite state maintains, the body attempting to compensate for the excessive loss of carbon dioxide by the excretion of an alkaline urine with a reduction in the ammonium salts and a relative increase in the urea excreted. It is not quite clear why in the case of the addition of abnormal acids to the blood, as in diabetes, the respiration should be so excessive that the alveolar air actually becomes reduced, as it might be expected that the reduction of the carbon dioxide in the blood which results would pre-

vent the breathlessness. Nor can it always be shown that there is an actual increase in the hydrogen ion concentration of the blood, even in diabetic coma. It may be that the abnormal substances produced, e.g. acetone, have a specific stimulating effect on the respiratory centre as put forward by Hurtley and Trevan, but the breathlessness may also be due to a purely local stimulation of carbon dioxide in the respiratory centre, since the acid-carrying power of the blood may be appreciably reduced. More recently the author has shown that in animals the extent to which the respiration is influenced by the impulses which pass up the vagi (see Hering-Breuer reflex) may be profoundly altered by conditions affecting the general sympathetic-parasympathetic balance. The evidence seems to suggest that the sensitivity of the respiratory centre to the gaseous content of the blood may be related to the autonomic nervous system. An increased sensitivity so brought about would certainly explain the hyperpnœa referred to above.

CHAPTER XXXIII

THE WATER CONTENT OF THE BODY

In order that absorption shall occur through the gut wall, the substance to be absorbed must be in solution. Water, the physiological solvent, is therefore an essential constituent of the diet. It can be demonstrated that food-stuffs are better utilized if the fluid of the diet is not unduly reduced. This finds popular expression in the idea that drinking with meals causes stoutness. The truth is that insufficient fluid intake may cause thinness.

The amount of fluid required for absorption is usually in excess of that needed permanently in the body and must therefore be got rid of. This is done mainly by the kidneys, skin, lungs, and intestines. The body, however, is economical in its working and makes use of the fluid excretion for other purposes. Thus the urine contains many substances which the body requires to get rid of, the sweat is utilized to keep the body cool, and the fluidity of the bowel contents is essential for adequate removal of the undigested part of the food.

Now the water available for all these purposes is limited by the amount taken in and the more that is utilized for one function, the less is there available for others. Thus, if a great deal of water has been required for the production of sweat, the less is available for the urine; the urine then tends to be unduly concentrated and for this reason we see the special liability to calculus in the residents of hot countries. Similarly, the obvious physiological treatment in cases of gravel or tendency to crystal precipitation in the urine is increased consumption of bland fluids. Intense diarrhœa also, or loss of fluid by the intestine seen typically in cholera, causes urine secretion to cease. Actually in this condition the blood is so deprived of water and becomes so concentrated that it is described as being tarry. It is doubtful if this fact is fully appreciated in ordinary cases of poisoning with severe diarrhœa. In such instances the consumption of enormous quantities of fluid is essential; otherwise fluid will be taken from the blood. In cholera the hypertonic saline treatment of Rogers depends on the fact that not only is fluid injected intravenously, but by increasing the saline content of it the osmotic pressure is so raised that the fluid cannot be removed so rapidly from the blood-vessels and the fluidity of the blood is maintained. Excessive loss of water in the urine is seen in conditions in

which the kidney requires water in order to get rid of certain substances, e.g. sugar, or when that organ is unduly stimulated, e.g. by urea. In the former condition we have the well-known thirst of diabetes produced in a way strictly analogous to the thirst of excessive sweating.

The production of thirst is one of the protective mechanisms of the body, as is the production of appetite. Appetite, however, is largely a question of habit and cannot be taken as a trustworthy guide of the individual's needs. Thirst, on the other hand, generally, but not always, is a better guide.

Thirst is essentially the result of diminished secretion from the salivary glands, and the effect of the dryness on the nerve endings at the back of the tongue. That this latter fact is so, is seen by painting the tongue with cocaine which rapidly abolishes the thirst in an otherwise thirsty person. The salivary glands are very rapidly affected by the slightest reduction of the fluid content of the blood such as occurs from excessive loss by one channel or another and act as an indication of the fluid need of the body. Paralysis of the salivary glands, and the thirst produced thereby are well seen after the injection of atropine which affects the gland directly. It is seen, for example, after operation where atropine has been administered (as a routine, by some anæsthetists) to diminish the possibility of vagal inhibition during anæsthesia, especially the first stage, or where it has been given to reduce secretion in operations of the nose, mouth or throat. Nothing better than personal experience can give full appreciation of the thirst after atropine which has the great disadvantage that the patient, if allowed to drink excessively, is unduly disturbed by the necessity of getting rid of the excessive fluid imbibed. This may have obvious disadvantages where quietness is essential from the point of view of the hæmorrhage of the operation, say in the nose. Treatment by painting the back of the tongue with cocaine is obviously indicated when the thirst is severe. The tissues and nerve endings at the back of the tongue may be dried by local applications. This occurs especially on the application of substances which normally withdraw water. Thus we have the thirst caused by the taking of salty foods, of alcohol and of sugar in the so-called mineral waters. In the latter case the addition of sugar is intentional by enterprising manufacturers to cause further thirst. It is thirst of this nature which may tend to cause a drift towards chronic alcoholism. In the latter condition the state is aggravated by diminution in salivary secretion.

Retention of excessive fluid in the body may be due to general or local causes. The fluid may infiltrate the issues as in *œdema*, or in serous cavities

as in ascites. The possibility that the plasma may become diluted in virtue of the loss of its protein is dealt with below under the treatment of nephritis.

There may be an upset of the mechanism by which fluid is retained in the blood-vessels. The elucidation of the mechanism we owe especially to the work of Starling, and it seems to be as follows: The capillary wall appears to be of the nature of a semi-permeable membrane, which will allow of the passage of crystalloids (e.g. salts and sugars) but not of colloids. Normally there is a balance of forces. On the one hand the capillary blood pressure tends to drive fluid out of the vessels, while on the other the osmotic pressure of the plasma proteins tends to prevent its leaving, for that of the tissue fluids is less than that of the plasma. Œdema may result from an increased capillary pressure—as would be brought about by a venous back pressure, from a lowering of the osmotic pressure of the blood by dilution (as in general water retention), or from an increased permeability of the capillaries which may permit the passage of proteins. In disease the last possibility appears to be specially important, for permeability may be altered by conditions such as anoxæmia, toxæmia, and some abnormal nervous states.

General retention is seen in acute and subacute nephritis. The fluid tends to accumulate in those parts of the body most dependent and where the subcutaneous tissue is loose and the circulation least efficient. Thus an individual often notices his puffy face, especially round the eyes, in the morning after getting out of bed. This disappears during the day and in the evening the ankles are seen to be swollen and "a ridge is formed on the top of the boot." In severe cases this œdema of the face may not pass off and, of course, does not if the individual is kept in bed. Death may be brought about by the more important parts of the body, such as the pericardium and the lungs, becoming œdematous, the individual drowning as it were in his own fluid.

The characteristic of œdema is that the fluid may be readily pressed out of the part affected. The sign of pitting on pressure is of great diagnostic value, as it is not given by conditions such as myxœdema, or fat, which may appear similar.

In *cardiac failure,* the œdema remains more fixed in position and begins in the more dependent parts where the circulation is deficient, and the venous pressure high. In reality this œdema results from the local causes at the site of the swelling. It has been shown by Bolton that this is not all due to a high venous pressure as such causing a high capillary pressure, but to an anoxæmia or want of oxygen causing increased permeability of the capillary walls from the resulting stasis, of which the high venous pressure is an index. It has, for

example, been shown experimentally that if the vena cava is obstructed the œdema is not synchronous with the time of the obstruction, but there is delay in its onset, and in its recovery, as would be expected from definite tissue damage.

The above state of affairs will occur whenever there is venous obstruction, and the blood is not allowed to return sufficiently rapidly from any part of the body. The return of the venous blood depends on a variety of factors, the heart, the veins themselves, the respiration, and the arterial pressure; failure of the latter two is almost impossible as it is incompatible with life, but failure of the heart and veins is comparatively common.

Cardiac œdema, as has been said, is not confined to any special area except that it is most marked in those parts of the body where there is most strain, as on the veins in the erect posture, i.e. those below the level of the heart itself. Thus, œdema of the ankle is often an early sign of cardiac failure and is best elicited over the surface of the malleoli. Attention has already been drawn to the importance of venous pressure as an index of cardiac efficiency. Not infrequently there may be a combination of factors as in chlorotic shopgirls. Here there may be a mild degree of cardiac inefficiency owing to the increased work necessary on the part of the circulation, increased dilution of the blood and local effect on the veins from the excessive standing.

Œdema in cardiac cases is often very persistent and taxes all the resources of the physician. The œdema may affect all tissues, and in the lungs predisposes to hypostatic pneumonia. This is a frequent cause of death in aged people who have been brought to bed from some other cause such as injury, for œdematous tissues have very little resistance to infection. It must be realized that cardiac œdema is often the result of myocardial failure without necessarily any preceding valvular disease and that the œdema with slight breathlessness on exertion (often taken for granted by the individual as a consequence of his age) may be the only sign of the condition.

Simple *failure of the veins* occurs when limbs have been kept dependent for an unusual length of time, as after marching. The hands even in a normal person may become sufficiently œdematous to be appreciated by the person affected. In the same way the feet, as is recognized by bootmakers, are distinctly larger at the end of the day, especially if the individual has been standing a great deal. It is a well-known fact that shoes become tight after an abnormal amount of walking and especially standing, in which, as there is little muscle movement, there is none of the compressions of the veins which facilitates the return of the blood. In these instances an unaccustomed strain has been thrown on the veins and some of the valves may have given way. We now know that

the veins do possess a definite vaso-motor mechanism under central control, but apparently, like all other mechanisms, it requires to be frequently utilized to act efficiently. As the individual becomes accustomed to a particular exercise or position, œdema is less readily brought about, provided, of course, that it is not allowed to persist in the first instance. Otherwise the subcutaneous tissue appears to enlarge, and, as in the case of the feet, the annular ligaments become stretched and permanent thickening of the ankles may result. A similar condition is also seen in horses and treatment by tight bandaging is obvious.

A similar venous stasis and anoxæmia of the blood-vessels results from any gross *venous obstruction.* In cirrhosis of the liver the portal system is affected, and the œdema is indeed a most serious symptom. Here the portal capillaries become extremely permeable from the obstruction to the veins of the liver and fluid accumulates in the peritoneal cavity in enormous quantities. Such a condition will be confined entirely to the portal area in whatever position the body is in, and there is no œdema of the ankles until the abdominal pressure becomes very high and the inferior vena cava becomes pressed upon, as is seen in pregnancy.

Any local pressure on the veins brings about the same result, the symptoms depending on the actual veins obstructed. New growths, glandular affections, such as Hodgkin's disease, produce symptoms in this way. The œdema, especially if unilateral or localized, may be of considerable diagnostic value in obscure cases, e.g. œdema of the face in thrombosis of the cavernous sinus, where it may be an early indication of the condition.

The permeability of the tissue capillaries directly or indirectly may be affected by *nervous* means, for we have evidence that the capillaries are under nervous control. In definite nervous lesions of the reflex arc, such as locomotor ataxia, œdema or even herpes may occur in common with the general trophic changes. In the same way from nervous changes as yet incompletely understood, we have angio-neurotic œdema, the œdema of neuritis or neuralgia, intermittent hydrarthrosis and the blebs of herpes zoster. Our knowledge of the laws which govern permeability of the capillaries, or indeed of any tissue, is so scanty that one dare not even make a suggestion as to how any nervous impulse should control the permeability of a membrane.

We do know, however, that *toxins* affect the capillary wall. Various wheals and swellings after the injection of toxins are produced in this way. The injection of histamine, nettle stings, bites of insects, certain articles of diet in sensitive individuals, all cause œdema. That of the chest wall in empyema may be looked upon as similarly produced. The transudation of lymph in inflammation

no doubt also depends on similar mechanisms. Lewis has shown that in those individuals whose skin vessels and local mechanism for dilatation are unduly irritable the œdema which makes dermatographia possible is apparently due to the formation of a toxin in the region of the stroke of the writing object. This he suggests may be one of the mechanisms which control local capillary dilatation and in such condition brings about the additional amount of blood which is necessary to deal with the toxin.

Finally, we know that the permeability of the capillaries is reduced in vitamin deficiency, as in scurvy and beriberi, in which latter the wet or dropsical form has long been a definite entity.

In all conditions of œdema, other than those of mere dilution, we have changes possibly only local in the normal water content of the tissues from change in the capillaries. This view is perhaps somewhat arbitrary. It is held by some that the real change is one in the tissue due to devitalization and the formation of substances which attract the fluid from the blood-vessels. The actual result is the same whatever view may be held.

Treatment.—From the point of view of treatment, the primary cause is most important. Removal of the cause is, of course, most desirable, but not always possible and local and general treatment has to be resorted to. Local treatment consists in removing the actual fluid accumulated, such as the tapping of ascites in liver cirrhosis. In this condition attempts have also been made to assist nature as in the Talma-Morrison operation by making an anastomosis between the portal and systemic venous systems. These, however, have only been moderately successful, although instances occur in which there has been amelioration to a considerable degree and even disappearance of symptoms for several years. In this category also is the use of Southey's Tubes, by which fluid is drained away from œdematous parts. Large quantities of fluid may often be thus removed, but it has to be remembered that œdematous tissue is particularly liable to infection. General treatment is more commonly used in cardiac and kidney cases. In the latter, the retention of the products of metabolism is even more important than the water retention and therapy concerns itself in increasing the excreting activity of the skin and the intestine. This is more fully dealt with in relation to kidney cases on page 141.

In cardiac cases there are several physiological principles which are essential to proper treatment. The pumping action of the heart, which is at fault, needs first attention and cardiac tonics require to be administered (page 143). If the œdema is severe the patient must be kept in bed to assist the venous return and in convalescent heart cases it is often surprising how difficult it is

to get the patient to understand this, for he feels comparatively well provided he does not do severe work. The longer, however, the œdema is allowed to persist the more difficult it is to get recovery, as the capillary wall apparently becomes more and more damaged from the anoxæmia which is itself aggravated by the œdema. On the other hand, œdema, if treated energetically and as soon as observed, clears up even in severe cases as if by magic. Anyone who has attempted to cure varicose ulcers will realize the lack of vitality of the tissues in which the venous return is impaired. The ulcer may heal while the patient lies in bed, but breaks down readily when he gets up. This, like the œdema, is all a matter of the oxygen supply to the tissue and this condition indicates the importance of keeping the feet up in œdema. This is well seen also in pregnancy when the venous return from the legs may be interfered with by pressure and the œdema in the feet is seen to come and go according to the extent to which the feet are kept up. In cardiac œdema there is every indication that the administration of oxygen would be of value, and Leonard Hill and his co-workers have obtained considerable improvement from immersing the patient in an atmosphere of oxygen by means of a bed tent.

In the treatment of œdema the effect of reduction of sodium chloride in the diet is well appreciated. It is of course necessary in the first instance to reduce the intake of fluid as far as possible, a point not infrequently forgotten, for the kidneys may be congested and every effort has to be made to reduce their work to a minimum. The blood contains normally sodium chloride to the extent of 0.9 per cent., and if it become diluted, the excess of water is rapidly excreted by the kidney. Obviously, then, the amount of salt in the body governs to some extent the amount of water held. If the diet contains salt the saline absorbed is but slowly excreted and in disease particularly slowly, as there is difficulty usually in excreting chlorides. But if, on the other hand, the salt is cut out of the diet as far as possible all the fluid taken in simply dilutes the blood and is excreted. Of course a certain amount of fluid has to be taken for purposes of the absorption of nourishment and excretion. Further, in excreting the fluid a certain amount of salt is lost and still more fluid will have to be excreted to maintain the normal concentration of the blood. Actually this does not go on indefinitely as the kidney ceases to excrete sodium chloride when the salt in the diet is reduced. Excessive excretion, on the other hand, by the skin may actually take place to an extent which may lower the salt content of the body to a danger point, as will be seen below. The procedure, however, of lowering the salt content of the diet is of obvious assistance in the elimination of excessive water from the body.

It is equally true to say, as pointed out by Maclean, that the amount of fluid in the body regulates the excretion of salt. When water is retained in the body it is retained as saline and hence in any condition of an œdematous nature, e.g. pneumonia, there is a retention of chlorides in the urine. It will be obvious that there is no necessity to restrict the chlorides in the diet if there is no œdema.

Recently more attention has been paid to the protein of the diet. It had commonly been considered that as the kidney was an important organ in the excretion of the products of tissue metabolism it ought to be spared such work and protein should be reduced to a minimum. In chronic parenchymatous nephritis, however, it has been definitely proved that there is an excessive loss of the plasma protein, which will lead to a fall in the osmotic pressure of the blood and to œdema, which will be increased by reduction of the protein in the diet, as emphasized by Epstein. Where there is excessive protein loss there should be no reduction of diet in this respect, and this is borne out by the observations of Maclean.

Important, too, is the elimination of water by the skin, and this can be brought about by keeping the surface of the body at a high temperature. Hot packs stimulate the skin generally, but hot air baths are best for the excretion of water, as the dry air can take up more water vapour. A bath of this kind can readily be improvised by hanging electric lamps inside a cage which is covered by blankets or preferably by a piece of asbestos sheeting. By using the modern gas-filled lamp fewer are required than if the older varieties are used. A patient under such treatment should receive frequent sponging or real baths. In hot air baths, salts may become deposited on the skin, and not only will they be irritating but they will interfere with further skin action. The dilatation of the skin vessels in cardiac cases is also of value in that it enlarges the capillary area, and by reducing venous pressure relieves the heart. Measures must be taken to keep the skin warm, not an easy matter, for the patients are often propped up owing to breathlessness.

The extent to which sweating will occur under conditions of high temperature does not appear to be limited, as in the cases of water loss by the kidney and by the salt content of the body, as remarked above. Provided sufficient fluid is taken to maintain the fluidity of the blood, sweating may take place to an extent which is actually dangerous, because of the excessive loss of salts. Such a condition is erroneously known as "water intoxication," and is found among those who work in deep salt mines in America.

The use of drugs to stimulate sweating, such as pilocarpine or salicylates,

is of advantage. The former, although possible in kidney cases, cannot be used in cardiac cases because of its depressant action on the heart by vagal stimulation.

The kidneys should also be stimulated, the common cardiac tonic, digitalis, being of value. As a diuretic urea is much the more efficient and has the advantage of being Nature's remedy. The caffeine series is also useful, but probably more irritating. The commonly used diuretin is theobromine-sodium-salicylate.

The intestines may also be utilized as a channel of getting rid of excess fluid. Any vegetable purgative may be used, and compound jalap powder has considerable reputation. Sodium sulphate (Glauber's salt) is most efficient and is a good diuretic. The purgative saline must be given in concentrated solution in contrast to that given in dilute form, purely to move on the intestinal contents. Brisk purgation is not a method which can be prolonged indefinitely.

From what has been written regarding the factors maintaining a balance between the amount of fluid in the blood and tissues, it will be clear that to promote the flow of fluid from the tissues into the blood it is necessary to increase the osmotic pressure of the blood or to lower the capillary pressure. The former is accomplished by the brisk purgative, since fluid becomes withdrawn from the blood into the bowel. In the severe diarrhœa of children the blood may become very concentrated, and those who suffer from the polyuria of chronic nephritis tend to have somewhat dehydrated tissues.

A reduction of capillary pressure should on physiological grounds be brought about most effectively by venesection. The fall of arterial pressure is largely recovered from, but the venous fall is prolonged. This will not only relieve the heart but will also drain the tissues. As in chronic cases at least there is often an increased number of red corpuscles, blood can therefore all the more readily be spared by the patient.

CHAPTER XXXIV

THE TEMPERATURE OF THE BODY

By being maintained at a constant temperature, mammals are enabled to work under very variable climatic conditions. To enable them to do so a special mechanism has been developed. They differ from the cold-blooded animals in that they are able to limit heat loss, while the latter, although they produce heat, are rapidly reduced to the surrounding temperature.

The normal temperature of the body is the result of a balance between heat production and heat loss, both of which are variable. The balance in man is adjusted at 37° C. or 98.4° F. This may be obtained in the rectum, while that in the mouth is about a degree lower, and that of the axilla lower still. The sublingual temperature, with the mouth closed, is probably the most trustworthy for general purposes. If the respiration is excessive, even in nasal respiration, there may be an appreciable lowering of the temperature recorded by the entrance of cool air, a point to be noted in taking the temperature of breathless or hyperpnœic patients. There is also an appreciable diurnal variation, the temperature in the early evening or late afternoon being about 1° higher than it is in the early hours of the morning. The general variation is such in different individuals that the clinical normal may be considered to vary between 97.8 and 99° F. The diurnal variation depends to some extent on the habits of the individual, and those who habitually work at night may have the reverse of the above. It is considered that this is due to intake of food and increased metabolism during the day, but no doubt sleep itself is a factor, for metabolism is noticeably reduced in sleep, as is also the activity of the nerve centres. The diurnal variation becomes exaggerated in certain conditions, typically in tuberculosis or chronic bacillus coli infections, and may be looked upon as due to the general irritability which occurs. On the other hand, the swinging temperature of acute septicæmia is diagnostic of the presence of pus; although the intermissions may be very great, they do not necessarily observe accurately diurnal variations, and are much more irregular.

Heat production has already been discussed under the principles of feeding and those governing growth, where the heat produced in the metabolism of the essential organs is fairly constant in the same individual for long periods.

The heat which is associated with muscular work depends on the amount of work done. That excess heat is produced by muscular work is well known. Even in the resting individual, provided he is not asleep, skeletal muscles play a considerable part in the production of heat. This is seen to be associated with the tone of the muscles and integrity of the reflex arc. If in an animal the nerve endings of the motor nerves are paralysed by curari and artificial respiration maintained, there is an appreciable diminution in heat production. Similarly under anæsthesia or alcoholism much less heat is produced and thus we see the necessity for keeping an anæsthetized person warm, the more so as it is now known that a fall of body temperature may add greatly to the risks of surgical shock. It has also long been known that alcoholics are especially liable to suffer from the effects of cold. The same applies to any nervous condition or to any injury to the nervous system in which muscle tone is reduced. Especially was this importance seen in the severe shock after wounds in war-time where it was found that the keeping of the patient warm was of primary importance.

This is to be explained by the fact that cold tends to exhaust the suprarenals (Cramer). It has been amply shown that these organs are concerned with the protection of the body against toxic products which produce shock, e.g. histamine (Kellaway and Cowell).

In cold weather the heat production is raised by increased muscular tone. It may be sufficient to bring about shivering, which is really a reflex mechanism or an effort of Nature to maintain body temperature under the control of the heat-regulating centre. The fact that greater activity is necessary to keep up the body temperature in cold atmospheres has probably been one of the most important factors leading to the superiority of the races of the cooler climates. The feeling of lassitude on a hot day compared with the invigorating effect of cold is appreciated by most people accustomed to outdoor life.

The production of heat depends, for the most part, on the need of the individual to do muscular work. In maintaining a balance, an automatic arrangement is necessary for the regulation of the heat loss. This is effected by means of the heat-regulating centre. The centre is situated in the corpus striatum, which, as we shall see later, is the region in which all the centres peculiar to the higher animal seem to be situated. The centre reacts to changes in the temperature of the blood and varies the amount of heat lost by the body. This can readily be shown experimentally by heating or cooling the blood passing to the brain and observing the reactions produced.

Heat is lost for the most part through the lungs, and the excreta, but especially by the skin. In dogs, whose skin is not so active in this respect, as they

have no sweat glands (except on the pads of the feet), the respiratory tract is the more important. It is a familiar fact that a dog lying in front of a hot fire may pant in order to make maximum use of the tract as a means of heat loss which is brought about by the vaporization of the water and the heating of the expired air.

In man, however, the skin is much the more important and it is the skin mechanisms which are varied by the activities of the respiratory centre. The skin is for this purpose supplied with an enormous number of blood-vessels, and when they dilate, an increased amount of blood comes into comparatively close contact with the cool surface of the body and loses heat by conduction and radiation. To make up for this skin dilatation and to maintain the total size of the vascular bed reasonably constant, constriction of vessels elsewhere has to be brought about. Individuals, therefore, whose vascular reflexes are in poor condition, and whose internal blood-vessels do not correspondingly constrict, suffer from what may be described as relative hæmorrhage and fall of the aortic pressure. They notoriously suffer from faintness in hot weather or in church.

In addition to loss of heat by radiation and conduction there is loss of heat by the evaporation of the sweat, the secretion of which is stimulated. This mechanism will be particularly useful in hot atmospheres in which conduction and radiation are reduced. The heat lost by evaporation of sweat, therefore, depends on the humidity of the atmosphere. Here we find the reason why the inhabitants of humid climates and districts tend to be less active (i.e. and produce less heat to be got rid of) than others who live in dry areas, and it is a familiar fact that a hot and wet muggy day is very enervating. During the War, the effects of a hot humid climate were well seen in Mesopotamia, where cases of heat stroke from excessive heat retention were common. Sweating goes on normally in all of us, but it is only when it is produced at a greater rate than it can evaporate that we appreciate its existence. This is seen in the fact that more urine is passed normally on a cold day. Sweating, like the dilatation of the skin vessels, depends on the stimulation of the autonomic nervous system under the influence of the heat-regulating centre.

It is obvious that individuals differ considerably in their powers to lose heat. Tall thin men can lose more heat by conduction and radiation than short stout men whose surface is not only smaller but whose heat loss is also diminished by subcutaneous fat. The latter then require greater activity on the part of the sweat glands and the greater discomfort of such individuals on a hot day is readily observed.

The power to regulate temperature depends no doubt also on the speed

with which individuals can produce heat and to the condition of the vascular reflexes. The latter can be demonstrated to deteriorate appreciably if not utilized. By proper training and a reasonable amount of exercise great benefit often takes place. It is well known that those who take little exercise are particularly liable to feel cold and also to suffer from disease. We are all familiar, too, with people who wear an enormous amount of clothing even in summer. On the other hand, the dress of modern woman would have made her grandmothers shudder and indeed would have killed them had they attempted it without due acclimatization.

When the body surface is exposed to cold the blood-vessels of the skin close down and the skin becomes pale. If, however, in the closing down of the arterioles, some of the blood becomes entrapped in the capillaries, it loses its oxygen, and gives a blue appearance which is particularly well seen if the circulation is not good. The skin becomes rough from the production of the so-called goose-flesh, a survival no doubt of the mechanisms of lower animals whose hairs stand out to entangle greater amounts of air in cold weather. Sweating is in abeyance.

The amount of heat which can be gained or lost by exposure of a part to undue cold or heat is surprising and of recent years has been accurately investigated, especially by G. N. Stewart. By placing the hands or feet in cold water more heat can be lost than is produced by the body at rest and in this lies the truth of the popular fact that wet feet or wet clothes bring about various infections, since a lowering of the body temperature reduces resistance. In these instances the lowering is brought about by excessive evaporation. Similarly, excessive movements of air by increasing evaporation and conduction by changing the air in the immediate contact of the body, increases the heat loss, and herein lies the danger of draught which then depends on the speed of the inrush of air. A fully open window, for example, although it brings in just as much air, does not cause so much draught as a window a little open through which air enters at a much more rapid rate and which will cause much more cooling of the body if the individual be in the rapid current of air. The tendency to chill after a hot bath has been recently shown to be due to the lowering of body temperature as a result of paralysis of skin vessels which remain dilated in spite of excessive heat loss. Similarly, alcohol may, by leading to capillary dilatation of the skin, bring about excessive heat loss, although, as is the case after a hot bath, the superficial dilatation of vessels may give a pleasant sensation of warmth. Such instances show the importance of the maintenance of body heat in keeping up resistance against infection. We have seen how the

eating of protein by increasing the heat production is of value in this respect. At the same time it is, however, very clearly shown that if the body, especially the mucous membranes, are in a physiological condition, considerable lowering of temperature can take place without infection occurring. Thus in war-time men were often exposed to cold which would almost certainly have had a very serious effect in civil life. Local injury or fatigue have a similar effect in localizing infection when the blood contains pathological organisms, e.g. tubercle.

After exposure to cold the ideal method is to heat up the body as rapidly as possible and muscular exercise is usually available. Thus sportsmen may continue to expose themselves to conditions of heat loss, e.g. from wet garments, provided they keep moving, and it is only when a halt is called that there is a danger of a chill.

Local heat is in the same way very effective in raising body temperature and there is evidence that the anti-bacterial power of the blood is increased when the body temperature is increased. The beneficial effects of a hot foot bath, poultices and the like are thus explained, although from this point of view the exact situation of the poultice does not appear to be essential.

Human beings rely to a great extent on *clothing* for the prevention of heat loss (this is dealt with further on). Ideally the skins of animals are to be preferred, and it will be noticed that such "apparel" entangles a maximum amount of air and is extremely light. These are the essentials of clothing and in the maintenance of warmth it is the retention of a layer of warm air near the body which is most important. At the same time, the clothes must be so constructed as to interfere as little as possible with evaporation, and here lies the disadvantage of the wearing of rubber or oiled silk garments, although when it is very desirable to retain heat it is not usually desirable also to sweat.

The natural products, wool and hair, supply the necessity best as substances from which clothes should be made, and they have the advantage of being better non-conductors than vegetable products or silk. The looser woven the material is the better, but here we must not confuse warmth with wear. Many of the more expensive methods of weaving and of material have no advantages over cheaper varieties of clothing as regards warmth, although they wear better. From what has been said about the entanglement of air it is evident that two garments are much more efficient than one of double thickness, provided they are not too open at the free edges. Two cotton or silk garments are then very efficient articles of clothing, and but for this it is difficult to see how the modern woman would keep warm at all. In this respect it will be noted that the dress of woman, like Highland dress, is concentrated at the waist and experience of

the latter readily makes the wearer appreciate that the chilliness of the kilt is much more apparent than real. The wearing of so-called cholera belts signifies the importance of keeping this particular region of the body warm, for the alimentary canal is a region especially liable to be infected as the result of cold. The production of diarrhœa or the return of symptoms after an attack of dysentery which may follow a cold bath or sea-bathing has long been recognized.

The subjective *sensation of temperature* is, however, quite a local matter and bears no relation to the temperature of the body. We appreciate heat and cold by groups of special nerve endings in the skin which we know as the hot and cold spots. We may feel generally quite warm and have a normal temperature, yet one part of the body may be intensely cold. Of more importance, however, is the fact that substances which stimulate the skin give a feeling of warmth. Rough garments are considerably warmer than smooth garments for this reason. There can be no other explanation of the predilection some people have for coarse undergarments. It is even possible to feel warm although the body may be actually losing heat and such a condition is produced by exposure after taking alcohol or a hot bath. The pleasant afterglow which is experienced is merely the result of the dilatation of the skin, blood-vessels and the effect of the hot blood on the nerve endings. Actually it cannot be demonstrated that alcohol does anything but appreciably increase the heat loss and the use of alcohol as a protection against exposure depends on other factors (page 314).

Fever.—A rise in body temperature above normal is probably one of the most reliable pieces of clinical evidence of the existence of a pathological condition. It results usually from the introduction into the body of bacteria, but that bacterial toxins will suffice is seen in such a procedure as anti-typhoid or tuberculin inoculation.

The relationship of organismal invasion to fever is shown in malaria where the fever in the different types corresponds with the liberation of new crops of organisms into the blood-stream, as demonstrated by a blood examination. It has been suggested that the fever is brought about as the result of protein destruction. That there is excessive protein breakdown in the condition is undoubted. Whether this is primary or secondary to the fever is not at all clear. That it is secondary is suggested by the fact that protein destruction may be largely prevented by feeding with carbohydrates and that experimental high temperature increases protein metabolism. The advantage of a carbohydrate diet in fevers must be noted. On the other hand, the fact that injection of foreign protein may produce fever as in anaphylaxis suggests that fever fol-

lowing an infection may be due to a similar breakdown in protein. In anaphylaxis, however, there is so much disturbance, especially of the vascular system, that one cannot lay stress on this point.

From first principles, it may be due to increased heat production or diminished heat loss, but these two factors are much more interdependent than at first sight appears, since a rise of body temperature due to diminished heat loss or any other cause must result in an increased heat production consequent on increased metabolism.

But that increased heat production alone is not sufficient to produce fever is evident from the fact that conditions where there is a much greater increase, such as exercise or exophthalmic goitre, do not bring about fever. Further, anaphylactic fever is said to be accompanied by diminished heat production.

That there is diminished heat loss in fever is undoubted and there is general agreement that this is brought about by vascular changes and a reduced flow of blood to the skin. When the body deals with any toxic substance blood is drawn to the part. This is evident, if the lesion is near the surface, from the typical heat, redness, and swelling which with pain are four of the classical signs of inflammation. An additional supply of blood is also necessary for the toxin-destroying and eliminating organs. In order to supply this blood since the amount in the body is limited, there is, as in hæmorrhage, a diminished blood supply to the skin. It has been clearly shown by G. N. Stewart that a diminished flow through the hand occurs in fever. If the condition is of a mild degree, the individual may be described as merely "looking pale," but if more severe, he may, as a result of diminished flow to the nerve endings in the skin, feel a sense of cold or chilliness which is often experienced at the beginning of infection, such as influenza or pneumonia. At the onset of a malarial attack the patient is extremely pale, even blue, and there is actual shivering although even at this stage there is a rise of body temperature. A similar state of affairs is seen in the rigors of pyæmia. An interesting point has been drawn attention to by Cramer, namely, that the conditions which present themselves in the early stages of fever are closely akin to intense action of the sympathetic, such as would occur from adrenaline secretion, evidence of which he has brought forward.

Although the heat loss may be thus diminished heat continues to be produced, and if retained in excess, metabolism is stimulated, producing more heat. There comes a point, therefore, when the effect of the rise of temperature gains the upper hand and the skin mechanisms for loss of heat are brought into use. The skin becomes very hot and may at first be quite dry. The heat-

regulating mechanisms are not really thrown out of use as has been imagined, for the body can be shown to react to changes in external temperature even during fever. It appears, however, to be set at a higher level and the reason for this seems clear. There is set up an antagonism between the heat-regulating mechanism requiring blood to be sent to the skin and the causal agent which requires the blood internally. It is not until the temperature is appreciably above normal that the heat-regulating mechanism succeeds in getting the upper hand. Thus we see that in conditions in which there is an intense vaso-constriction with, say, shivering, there must follow an enormous rise of temperature to counteract this, as is well seen in the typical rigors of pyæmia and malaria. It seems also possible that the larger and more vascular the area affected the greater the liability to high temperatures. If little local reaction is set up there is, on the other hand, seldom much fever. Further, we see that where there is intense skin reaction, as in skin diseases, fever is usually absent. Where the condition, however, is not confined to the skin, as in the exanthemata, fever is common, although in some conditions, such as small-pox, the appearance of the rash is associated with a decline in the fever until there is an absorption of toxin from the postules.

Further, a point indicating the vascular element, is the fact that a cold bath given to a typhoid patient does not lower temperature so well at the beginning of the disease as it does at the end, when the typically large diurnal variations are seen. This would be expected, as there is so little blood in the skin to be cooled at the early stage.

The above hypothesis is a simplification of that of Barbour and his coworkers, to whom we owe much on this subject. He suggests that as a result of the infection there is a shift of the water to the tissues from the blood, which therefore becomes concentrated. In the reduction of blood volume, blood is no longer available for the skin vessels, which brings about the sensation of coldness with further vaso-constriction in the skin with heat retention. Much weight has been placed on the increased concentration of the blood. Increase in the cell content of the blood would readily account for this, and we know there is often an enormous leucocytosis and increase in the red cells while our knowledge of the normal variations in the plasma is as yet very scanty. It is difficult also to understand this claim to increased concentration, in view of the reduction of the chlorides which are normally the most abundant salt in the blood. We also could presume that according to Barbour's hypothesis the drinking of large quantities of fluid would reduce the concentration. Conditions which bring about concentration of the blood, such as hypertonic saline, certain

purgatives and concentrated sugar solution, do bring about fever and may do so probably by increasing the difficulty in sweating, but in fever the concentration, if it exists, may be due to loss of water through the skin. This is suggested by the fact that there is diminution in the secretion of urine. The appearance of salts from the evaporation of sweat on a dry skin suggests that the insensible perspiration in fever may be greater than normal. What exactly happens to the sodium chloride which leaves the blood has yet to be shown and it has to be demonstrated that it takes water with it, but until we know this the water shift hypothesis appears very uncertain, nor does there appear to be any necessity for such an elaborate explanation when a simple vascular one is available.

The beneficial effects of a cold bath in high fever are then evident, as by the cooling of the skin less circulation is necessary to keep down the temperature and more blood is available to deal with the infection. That simple constriction of the skin vessels can bring about a rise of body temperature was pointed out by early observers in the days when bleeding was a common practice. It was also noted by Lauder Brunton. In pneumonia, also, it is well known that the crisis is associated with the onset of perspiration, and at this time, too, the muscles, hitherto tense, and no doubt producing heat suggestive of protection against the cold of the skin, become quite flaccid, while the patient is obviously less anxious and ill.

Antipyretics lower temperature by reducing heat production, and some consider that quinine acts in this way. More commonly they increase the heat loss by local action, causing stimulation of the sweat glands, as with salicylates, or by acting through the heat-regulating mechanism. Phenacetin appears to act in this way, for its action is said to be abolished if the region of the heat centre is removed. How this occurs if the blood volume is appreciably reduced (as in the water shift theory of fever) is difficult to see. The patient would be liable to faint from a relative loss of blood. Further, it cannot be shown that all antipyretics dilute the blood, while how they can cause sweating, if the blood is concentrated, is difficult to understand.

According to the purely vascular conception of fever put forward above, the heat-regulating centre need only be made more sensitive to the heat, a method of pharmacological action which is well known.

Whether antipyretics are ever justifiable is very debatable, as the fever may be but an indication of a physiological mechanism. Whatever theory is held, it is much more in keeping with physiology to apply cold to the skin, as baths or packs. In carrying out such procedures the danger of excessive lower-

ing of resistance must be remembered. It is desirable to remove the patient from the bath when the temperature has fallen to 100° F., as a further fall may be anticipated. The importance of the administration of fluids in fever (even injections) cannot be over-estimated from a physiological point of view.

Low temperature is a rarer state than fever and is usually brought about by diminished heat production. This is well seen in myxœdema in which the basal metabolism may be very low. It may occur in any debilitated condition, so that the normal loss of heat may result in the lowering of temperature to a dangerous degree. In the aged, this is very marked and old people frequently die from infectious conditions, e.g. pneumonia, without any increase in temperature. Excessive rest from compulsory confinement to bed, say from an injury, results in lowered heat production and practically all patients in hospital not suffering from an infective condition have a subnormal temperature. A subnormal temperature in the morning associated with a slightly raised temperature in the evening is considered to be indicative of tuberculosis. It is usually found that these individuals, as stressed by Philip, have a considerably increased irritability of tissues generally. Thus the pectoral muscles, if stroked sharply, are seen to contract and the stroke itself gives rise to undue skin reaction. We can look upon this increased irritability as bringing about the excessive diurnal variations. Such a state would, of course, be expected in any chronic infection provided it was not too severe, and tuberculosis is the most common.

Lowered temperature from excessive heat loss is less commonly seen. It occurs in alcoholism and in chronic moist skin conditions. Babies less than a week old are specially liable to lose excessive heat and hence the necessity of keeping the newly-born very warm. Children have a comparatively large body surface and therefore have to have a more intense metabolism. It is very doubtful, therefore, if attempts at "hardening" are really justifiable, and it is most desirable to prevent excessive heat loss provided this does not actually amount to coddling. Later, when the vaso-motor and heat regulating mechanisms are fully developed, more liberties may be taken, apparently with even beneficial results, as in sanatoria.

CHAPTER XXXV

EXERCISE AND REST

THE EFFECT OF EXERCISE

Although it has long been considered that exercise is generally beneficial to the body, the lack of a definite scientific basis for this assertion has tended to bring about a disregard for it. In lay and even in many medical minds, exercise and fatigue are not clearly distinguished. Too often is the apparent impasse reached where the doctor finds himself and rightly, advising exercise to a patient who feels physically tired at the end of the day.

Within recent years our knowledge of muscular contraction has enormously increased; especially as a result of the War has it been possible for this generation to see the good effects of open-air life. Physical nonentities found themselves capable under the proper stimulus, of carrying out an amount of work which no amount of persuasion could have made them believe possible but a few months before. We now see that there is involved the great biological principle that structure is determined by function, and that function depends on the necessities of existence. This principle, we believe, has been largely responsible for organic evolution, but it is no less applicable to the individual organs of our body. Under conditions of civilized life our physical selves become less and less of importance for our existence and we find that we differ from the lower animals most greatly in respect of our brain structure which has indications of being the most highly evolved. Whatever the nature of our occupation our bodies and minds adapt themselves to a greater or less extent to our requirements. It is then most physiological that these requirements should be reasonably constant. Otherwise excessive strain may be thrown on individual organs and cause breakdown. A sedentary brain-worker is no longer adapted to meet physical emergencies any more than is a physical worker capable of doing a mathematical problem which he could do easily at school. In the latter instance we use the term "forgetfulness," but in the physical sense a similar term could quite readily be applied. Further, it appears very likely that the two processes, physical and mental, are essentially similar.

Whatever our occupation, however, there is a limit to physical unfitness,

for not only does every life depend on physical necessities, but the body is liable to disease and we shall see that by exercise the body creates a reserve which may be utilized—indeed, may be the deciding factor—in the maintenance of life under adverse circumstances produced by many pathological states. The subject is now considered in more detail in relation to those tissues in which the physiological effect of exercise is most evident.

The Muscles.—The voluntary muscles we know to be bundles of muscle fibres, each fibre capable of exerting its own tension independently. The actual arrangement of the fibres varies according to the situation of the muscle. Thus if a wide range of movement is desired the fibres are long and more or less parallel, whereas if a maximum tension with a minimum of shortening is required, a large number of fibres are inserted into a median raphe or long tendon, running almost the whole length of the muscles, as in those affecting the jaws. Experimentally the number of fibres utilized depends on the strength of the stimulus provided the amount of work to be done is constant. What is more important, however, is the fact recently shown by Fenn that the muscle adjusts itself to the work to be done after the contraction has already begun. In a manner not yet understood some local stimulus is set up by the load which causes the muscle to do more work. If the work is frequent, hypertrophy, i.e. increase in the number of muscle fibres, occurs. It seems reasonable to believe that this is the result of the stimulus set up by the load referred to above when the work demanded is in excess of the normal. In doing light work there is excellent evidence, not only that all the fibres of the muscle are not used, but that those required are utilized in rotation. For example, a pound can be held up in the hand for a longer period than a stone (14 lbs.), and if the weight is heavier it can only be retained for a very short period. In view of the fact that fatigue of individual fibres comes on comparatively rapidly, we must presume that in holding up the light weight for a long time groups of fibres have been utilized in turn. There must then be in the muscle some switch arrangement by which these groups are thrown out of or into action. The suggestion that such a mechanism does exist is supported by the existence of apparently similar processes in the capillaries, the alveoli, and the hot and cold spots of the skin. Possibly the products of slight fatigue allow the stimulus to spread to the other fibres. It is not, however, until all the muscle fibres of the muscle are fatigued that the contraction is diminished and the sense of fatigue appreciated.

Fatigue.—In a biological consideration of muscular fatigue in man we must look upon the individual muscles of a certain group, say of the leg, as analogous to the relationship of the individual fibres to the muscle. We may

fatigue certain muscles, or certain groups of muscles. Here we find ourselves faced with another factor, namely, muscular adaptation, not only to certain movements but to a certain speed of movement. We are familiar with the fact that the slow walk of an invalid is much more fatiguing than a more rapid one. Similarly, a Marathon runner is by no means necessarily an efficient walker. Indeed, he finds running much less fatiguing than walking. He has, in other words, an optimum rate of contraction of muscle, and it can be demonstrated that at this rate less oxygen is required for the work. In average persons this is approximately at the rate of two steps per second, and it is interesting to note that the army authorities from experience and quite independently at an earlier date arrived at 120 paces per minute as the optimum rate of marching. There is, no doubt, an appreciable individual variation in this respect, as the performance of a Marathon runner suggests. Greater facility in co-ordinating muscle groups no doubt also plays an important part. The department from which this volume was written has the misfortune to be on the third storey, and some 120 steps from the ground floor, and it is common experience that although at first or after vacation it is a difficult matter to hurry up the stairs, in a few weeks the exercise becomes appreciably easier and is no longer accompanied by circulatory or respiratory distress, although actually after a vacation the individual may be much more physically fit in a general sense. It is obviously a matter of co-ordination of muscle.

These facts are of considerable importance in relation to training in general in that special training is necessary for a particular sport or exercise. It is a well recognized fact that the long-distance runner is seldom an efficient sprinter, and *vice versa*. In the treatment of obesity, too, these facts have to be remembered, as walking, in an individual accustomed to this form of exercise, ceases to be a method by which large stores of energy can be got rid of (see page 208).

Muscular fatigue is, then, a local condition and although the result of muscular movement, yet is quite distinct from exercise in the general sense, although the latter, if excessive, may bring about fatigue. It is possible to fatigue certain muscles quite easily and not appreciate the beneficial effects of exercise. Exercise is much more general in its conception and can only be held to be taken when the muscular movement has been sufficiently tempered to cause increased activity of the circulatory and respiratory systems. In an ideal exercise all the muscles of the body are used to a moderate extent and a sense of pleasant fatigue, not localized to any special group of muscles, should be experienced.

Now it has been shown by Krogh that in exercising a muscle a large number of capillaries previously closed become opened up. This must result in a

washing-out of the products of metabolism and in the utilization of stores of energy which give a sense of freshness and fitness in the muscles comparable to that experienced when one washes one's face in the morning. The blood-flow through a part in use is also increased by means of the Lovén reflex, by which the sensory impulses bring about dilatation in the organ from which they proceed. This reflex, which is quite clearly established (Bayliss), appears to be of the nature of an axon reflex (page 35). The impulse passes up by the afferent fibre towards the posterior nerve root, but at some point the stimulus passes to the outgoing vaso-dilators which accompany the sensory nerves.

Massage and electricity bring about essentially the same thing, and they are often possible when exercise is not as after injury. In this latter respect there can be little doubt that bed exercises are not sufficiently utilized to maintain general fitness when confinement to bed is necessary. Movements against resistance can readily be made even in the recumbent position and the majority of the body muscles can be so exercised. Electricity has many fashionable adherents and may act in several ways. It may actually stimulate the muscles to contract, as in the Bergonie chair treatment, or by the sensation it produces cause the patient to contract muscles or it may stimulate vaso-dilators, if it is of a certain quality, as the experiments of Bowditch and Warren suggest.

Exercise must then be in proportion to the musculature of the body. In our cities thousands of individuals leading active mental lives have little exercise and apparently do not suffer. The truth is that the general musculature is small and less exercise is required. Thus an individual accustomed to much exercise suffers appreciably if compelled to lead a more sedentary life. Many felt this on returning from military service after the War. Gradually, however, the muscles degenerated to their civil requirements and there was no longer the same necessity for exercise, a moderate amount sufficing to give a sense of physical well-being. Unfortunately, in the same way, it is possible for an individual to feel well with little or no exercise, and he is led into a false sense of security as he becomes less and less efficient physically and also less capable of resisting disease. Not only do the skeletal muscles become reduced but also the efficiency of the other systems, especially the circulatory and respiratory, which are essentially the servants of the muscular system. Recent work goes to show that the circulatory, respiratory and autonomic nervous systems are primarily designed to serve the physical needs of the body, especially in relation to the supply of oxygen and elimination of carbon dioxide. But what is more important: should any breakdown occur in the tissues or mechanisms responsi-

ble for the supply and elimination, Nature utilizes the mechanisms primarily designed for exercise to make up for the deficiency. For example, should the blood become inefficient, the circulation becomes more active, or if the circulation fails the respiratory efficiency increases. The less then the margin kept utilized by exercise, the more liable is the individual to be overwhelmed by an acute breakdown, although when the latter is less acute the body may get time to mobilize its defences. This will be seen to be specially the case in relation to the circulation.

Circulation.—The effect of exercise on the circulation is to increase the amount of blood passing from the lungs to the tissues in a given time, and thereby the supply of oxygen. The mechanism by which this is brought about has already been dealt with. Exercise, for various reasons, produces an increased venous flow and pressure, and by increasing the sympathetic and diminishing vagal tone increases the cardiac rate. These, together with the increased inflow, cause an enormous increase in cardiac output. As with the skeletal muscles, the heart, if the exercise is habitual, adapts itself to the increased work, and if necessary hypertrophies to deal with the greater load. One of the aims in athletic training is to produce an increased cardiac efficiency. A similar hypertrophy of one or more chambers of the heart occurs in valvular disease. Here the increased work is brought about not by the increased filling but by increased resistance and deficient emptying. This latter, added to the normal filling, brings about the same effect as increased filling would do. The muscular hypertrophy is compensatory, and it is evident that a greater margin of compensation may be produced by carefully graduated exercises. This has been considered in relation to cardiac efficiency, and is the basis of modern treatment in cardiac disease. As with skeletal muscle, exercise is necessary to keep the cardiac muscle efficient. In cardiac disease too often does the patient take excessive care of himself. The beneficial effects of exercise are then evident, provided the exercise is adjusted to the capabilities of the individual.

Exercise also increases the vaso-motor tone.

There is also a marked increase in vagal tone, which makes itself evident in the slow pulse of those who habitually take severe exercise. Probably the increased peristalsis which exercise brings about may be partly of a similar nature. The same may be said of the fact that diabetics require insulin when taking exercise (Lawrence), since we know that the pancreas is under vagus control. How exercise products the increase is a very interesting problem.

The effect of the anticipation of exercise in the circulation has been discussed in relation to the rate of the heart.

Respiration.—Exercise, by causing an increased production of carbon dioxide and utilization of oxygen, necessitates a great increase in the efficiency of the respiration (Chapter XVIII). When the exercise is habitual, however, there is a permanent increase in respiratory efficiency. The chest and lungs become larger and there is, in consequence, not only an increased respiratory surface, but also a more efficient replacement of alveolar air, as indicated by the increased vital capacity and chest expansion (page 154). In other words, an increased amount of blood can be aerated in the lungs in a given time without undue hyperpnœa. In disease, should any pathological condition arise which would lead to breathlessness, the normal margin of reserve is taken up, but it will be obvious that the more exercise has been taken the greater reserve there is to fall back upon. Hence, we see the value of strenuous games at an age while the thorax can still grow. Similarly, breathing exercises and gymnastic exercises which enlarge the chest are also of value and are more possible often for children insufficiently robust to play games such as football. The latter, however, must be considered a much more physiological method of increasing the respiratory reserve than so-called breathing exercises, as the latter, although they may enlarge the chest cavity and possibly the lungs, cause a washing-out of the carbon dioxide from the body which is quite an opposite state to that produced by exercise in that it tends to depress the circulatory and respiratory mechanisms. Normally, increase in respiratory efficiency should be accompanied by increased cardiac efficiency, which latter does not occur with breathing exercises.

The Nervous System.—The effect of exercise on the autonomic nervous system has already been alluded to above, and as a large number of the skeletal nerves are utilized we may presume that they are benefited, although we know little about the mechanism of nerve conduction in this respect. There is indication, however, that hypertrophy of muscle brings about also hypertrophy of nerve. It is also clear that by the frequent use of certain paths in the nervous system the resistance in these paths becomes appreciably reduced and the movements concerned become easier to perform. This is particularly the case in relation to reflexes (see page 39), which play an important part in muscular exercise. To the sedentary brain-worker probably the most important action of physical exercise on the nervous system is the mental relaxation which is produced and which is often so difficult to obtain. Not only does the relaxation occur during the exercise itself, but sleep is promoted, which is essential to active life of any kind.

Just as physical exercise is of benefit to the body generally, so mental exercise

benefits the brain, and it is a well accepted fact that, within physiological limits, the more mental work an individual has to do, the more he finds himself capable of doing. It is a common experience that the results of examinations are better in the heavier terms than in the light ones, and we are often surprised at the amount of work individuals, whose time appears to be already much occupied, find time to do. As yet, we are quite unable to understand how this occurs, but from general biological principles, especially the fact that the brain of man has developed a surface much in excess of any other animal, even allowing for differences in size, we may assume that it "hypertrophies" with mental exercise just as does any other tissue. We do not know the nature of this hypertrophy, which obviously cannot be an increase in bulk, although it may be conceivably an increase of surface at the expense of the less utilized areas.

Digestive and Other Organs.—Exercise must also be beneficial to all organs responsible for metabolism, as the essential *raison d'être* of metabolism is the provision of energy for transformation into external work. The matter need not be dealt with in detail, but we are all familiar with the stimulating effect of exercise on our food consumption and digestion. Important, too, is the beneficial effect of exercise on the bowel movement, although how this is caused is not quite clear. There is, however, evidence (McDowall) that this is brought about by an increased action of the parasympathetic generally, which occurs after exercise, possibly through an effect on the acid-base equilibrium of the body. Such an increased parasympathetic action is proved in relation to the circulation and it seems from the evidence likely that by a similar action in relation to the digestive tract, the efficiency of the digestion is adapted to the energy requirements of the individual. This has been considered in more detail in relation to the chapter on the "Autonomic Nervous System" and is supported by the effect on intestinal movements of mental states and endocrine extracts. No doubt also the increased action of the abdominal muscles plays a part. Whenever any organ is used it increases its efficiency and if necessary increases its size. The exact stimulus to such local growth is not known, but it seems that whenever work is thrown on an organ to an extent that all its available reserve is used, hypertrophy occurs to provide a reserve and so to make it possible for different parts of the organ to rest, since, as we know, intermittency of action may be considered a law of Nature.

Exercise also by producing carbon dioxide and lactic acid brings into operation the mechanisms responsible for the maintenance of the body neutrality. Indeed it may, with justification, be considered that these mechanisms are rendered necessary by the possibility of severe exercise in the preservation of life.

As body neutrality is of considerable importance in disease it has been considered in a separate chapter.

THE EFFECT OF LACK OF EXERCISE

To appreciate the beneficial effects of physical exercise is but to appreciate the deleterious effects of lack of such exercise. We have noted that structure is dependent on function. It is a further biological principle that disuse leads to degeneration, and in an attempt to adjust organs to the requirements of the individual disease may be brought about. Every tissue may suffer to an extent which is not fully appreciated. A most striking instance of this came to the notice of the author recently. It was the almost complete disappearance of calcification from the spinal column of a monkey which had been closely confined for several years. The vertebræ could be cut easily with an ordinary knife.

With disuse the various systems gradually become less efficient. This we readily appreciate in relation to the muscles when we take part in any unaccustomed game. The muscles become stiff and painful, presumably from an accumulation of the products of the exercise which have not been adequately removed because of temporary inefficiency of the local circulation, and which cause an infiltration of fluid into the muscles. The pain must be considered to be caused by tension probably so produced.

There seems to be little doubt that those who have developed a large amount of muscle from special exercises are specially liable to feel the effect of lack of exercise.

Large areas of tissue must become relatively stagnant so far as circulation is concerned. This general feeling of lassitude is probably due in some parts to the substances produced as the muscle degenerates from lack of use. Specially important is the fact that similar degeneration tends to take place in cardiac muscle which has become hypertrophied as a result of valvular disease if the individual does not lead a moderately active life. Fatty degeneration and infiltration may also take place in a previously normal heart. In each case, there is an increasing possibility that the organ may become filled with more blood than it can pump out and may fail in attempting to do so.

Other parts of the vascular system also suffer. The power to regulate body temperature becomes, we know, seriously impaired by wearing excessive clothing. The extent to which human beings can utilize their skin to protect against cold is indicated by the fact that the inhabitants of Patagonia wore practically no clothes, although their climate is more severe than that of the British Isles.

Another instance of the loss of the function of the vaso-motor system is that of the caged rabbit, which, if the confinement has been prolonged and close, may die of cerebral anæmia if held up by the ears. This failure of the circulation to adapt itself to posture is also appreciated if for any reason we are confined to bed even for a few days. Not only do we lose the power of accurate walking from some loss of power to co-ordinate, but there is a sensation of "light-headedness" which is exaggerated in changing from the horizontal to the erect posture.

In surgery it is now realized that the inefficiency which may result from the prolonged lack of use due, for example, to a fracture, may be as important as the injury itself, and every attempt is made to maintain the condition of the soft parts by massage and movement.

The ventilation of the lungs also becomes reduced in those who take little active exercise, while we know that mental sloth is the forerunner of mental inefficiency. In industry it is recognized that skilled workers are less efficient than normal on Mondays, although it is agreed that a week-end break promotes efficiency—indeed, is essential.

Any dole-without-work system for relieving unemployment is obviously fundamentally unsound, through no fault, necessarily, of the recipient. There can be no doubt that the physical capacity to work becomes appreciably reduced and, until this capacity is regained, work is found to be extremely irksome. Any of us may undergo a similar experience if we embark upon an unusually energetic holiday and it is recognized matter for consideration in the training of Army recruits. In the more leisured classes games, possibly even dancing, form a convenient method of providing exercise. There can be little doubt that their increasing popularity amongst ladies has largely reduced the number of minor ailments which were the fashionable accompaniments of leisure in the Victorian era.

If insufficient exercise is persisted in there is inevitably a tendency to adiposity if the energy intake continues, and the laying down of fat in the various tissues, especially in the muscles and heart, leads to a still greater inefficiency and disinclination to work. Motor-cars have undoubtedly lessened the amount of exercise taken, and one has only to observe the general proportions of many of the occupants of cars in a fashionable area to appreciate this fact. Many doctors are similarly affected. Although their cars save them so much time it is often a curse in disguise from the point of view of exercise. The matter is dealt with more fully in relation to body weight.

Added frequently to lack of exercise is the effect of monotony, although clearly the two conditions may occur quite independently.

In concluding this subject we must note how often retirement from an active occupation is soon followed by death. Such a sequence must be considered quite unphysiological. Retirement should be gradual. As the flexibility, which is necessary in practically every walk of life, becomes reduced, less responsible occupations should take the place of the more serious, although even flexibility can be prolonged by exercise. The proof of such conclusions is that those who live longest are those who either never retire at all or those whose occupations are of such an easy nature that retirement is more nominal than actual.

THE NECESSITY FOR REST, SLEEP, AND INTEREST

Fatigue is the inevitable result of severe work. Rest is necessary as the physiological sequel to ensure recovery. No tissue in the body is constantly in use, and the more detailed physiology we know the more it becomes evident that this is true.

As already mentioned, certain capillary areas are known to shut down from time to time and also nerve endings. The necessity for rest is perhaps most evident in relation to muscle. A muscle can contract in the absence of oxygen, but it is necessary in the recovery process, and the amount of recovery will depend on the time between the contractions. The more frequent the contractions the less the recovery and in an emergency the muscle can actually go into oxygen debt (A. V. Hill). Fatigue, however, rapidly ensues and rest eventually becomes compulsory.

Such rest is quite local, but if the requirement is more generalized, sleep tends to be induced. Of the nature of sleep we know little. That there is usually a cerebral anæmia, and that there is a greater distribution of blood to the limbs is undoubted, and such anæmia would tend to bring about unconsciousness (page 6). These changes, however, may be the result rather than the cause. Although they appear to be the common corollary they are not essential, as has recently been shown by McWilliam, who brought evidence to suggest that the cerebral pressure may, in dreams and the like, become appreciably in excess of normal. There can be no doubt, however, that conditions which tend to bring about cerebral anæmia facilitate sleep, as is seen when we sit down in front of a fire after dinner, or where there is a minimum of external stimulation. Similarly, a monotony of stimulation has the same effect. No doubt the actual nerve structures involved become fatigued. The

most suggestive recent work on the subject of sleep has been that of Pavlov, whose experiments appear to indicate that inhibition, hypnoses, and true sleep are essentially similar phenomena of varying degrees of magnitude, and may be produced experimentally. He brings forward evidence which suggests that sleep is an inhibition of certain parts of the cerebral cortex and may be very localized. It has been found possible, for example, to produce an inhibition of the motor cortex in a dog so that the animal, although hungry, may not partake of food. There is much evidence which suggests that in sleep all mental processes are not closed down and the reverse possibility that certain individuals are often only "half awake" may have a scientific foundation.

Whatever its nature, it is generally agreed that sleep is essential to promote bodily rest, and during sleep all the functions are reduced to a minimum provided it is undisturbed by dreams. For the average person eight hours' sleep is ample, but it is evident that the more exhausting the occupation the more sleep is necessary. It is well known that some of our most active public men require at least nine or ten hours' sleep and have exceptional faculties for sleeping when not actually at work. Sleep, however, is a matter of habit and the more we have the more we want. It is possible to accustom oneself to extraordinary little sleep, and some appear to be capable of doing with comparatively few hours. Edison, the inventor, is stated to be one of these.

Sleeplessness is one of the curses of our civilization and it is specially evident in those who have insufficient or excessive bodily or mental exercise. Excessive bodily fatigue, which is painful, may result in sleeplessness; similarly, late suppers to those unaccustomed to them or strange beds, and all conditions, e.g. pain or the discomfort of a full bladder, which, in virtue of the sense of stimulation produced, bring about vaso-motor states preventing cerebral anæmia which, although not necessarily the cause of sleep, is a common, if not essential, corollary of it. Cold, for example, is probably one of the commonest and acts in this way. The skin vessels become constricted as a protective action against excessive loss of body heat, and in such instances the effect of a hot drink, preferably milk (as it also allays gastric acidity) and a hot-water bottle are often marvellous. Excessive mental activity, especially when associated with an impaired vaso-motor system, such as may be brought about by arterial sclerosis or mere lack of use, is also a common cause of sleeplessness. Worry is perhaps the most difficult cause to treat, and in the milder cases, light reading at bedtime to take the mind off more serious topics is often found useful. Alcohol, too, has many advantages in this respect. Its vascular action and the sense of well-

being it promotes both induce sleep. This sense of well-being is of more importance in relation to sleep than is often at first sight supposed, as not infrequently sleeplessness is at least made worse by the fear of sleeplessness, or lack of confidence in being able to sleep. The tendency to form an alcohol habit frequently contraindicates its being advised, and in such cases the more disagreeable hypnotics, e.g. paraldehyde, are prescribed. In no instance, however, should drugs be prescribed until the physician has considered the cause of the sleeplessness in the individual case and if possible dealt with it. Psychotherapeutic measures are of much value.

When, however, there is excessive energy output it may not be possible to obtain sufficient sleep for complete recovery. Each day's work is begun before the fatigue of the preceding day has worn off and slowly complete fatigue supervenes or a degree of inefficiency is produced which reduces the amount of work possible. This may occur as the result of excessive physical or mental work or both combined. The former was not uncommon in war-time when not only were there occasions of great physical output of energy but the opportunities of sleep were often very limited. In civil life excessive nerve strain in this way is common. The nervous exhaustion may be purely local, as is seen in the condition of writer's cramp, which results from excessive writing, and once established the condition may be extremely difficult to get rid of. More commonly there is a general local breakdown in which the individual is quite incapable of working or standing the mental strain any longer, and Nature enforces rest. Not infrequently such insidious fatigue is associated with monotony, as indicated above. A holiday is the natural and physiological antidote to such fatigue; even cessation of the usual work at the week-ends is of enormous value, and there can be little doubt that the moral obligation of keeping the Sabbath is really based on a physical necessity. The efficiency of skilled workers is reduced on Mondays or after holidays. On the other hand, without that holiday there is a gradual diminution in the total output per week. The holiday must, however, be suited to the needs of the individual and is quite distinct from that necessary to relieve monotony. A visit to an Exhibition may be of value to those who suffer from the latter, but it is of no use for those who require rest, just as rest is insufficient if revival of stimulation is required. Each case must be judged on its own merits.

More and more attention is now being paid to the alleviation of industrial fatigue which we may look upon as a mixed variety of fatigue. The elimination of unnecessary movements, the introduction of rhythmical and alternative movements, the provision of rest pauses, are all of value in preventing actual

fatigue of muscles, but, as we shall see, the mental state also requires to be studied.

The Necessity for Variety or Interest.—We are but creatures of our own physical environment, and although sometimes apt to forget that this is so, we are quite conscious of the effect of environment on others. In some of the earlier chapters we have seen how many of our actions and thoughts became purely reflex and adapted to our daily needs. Structure adapts itself to function, and, in the biological world in general, we see how plants and animals have become altered to suit the conditions under which they live.

Throughout all this adaptation there is one requisite factor, namely, stimulation. The plant is stimulated by its environment, and variation is brought about. In the same way, however original we may imagine ourselves to be, everything we say or do is the result of stimulation in some form or other. The primitive animal concerns itself chiefly with the necessity of preservation of the individual or the race, and, in doing so, a utilization of energy is necessary which, in return, necessitates a supply in proportion to the activity of the life.

Under many conditions of civilized life, however, stimulation is reduced to a minimum. To consider an extreme case, that of an individual in a factory spraying a piece of a toy with enamel. The picture is a drab one when considered as a form of human existence. A small chamber, partitioned off to prevent the enamel flying about, everything in front and at the sides black with enamel, the skin probably also coated, while on one side is a heap of pieces finished and on the other a heap to be done. The story of Dickens in his factory may yet be seen daily, although admittedly conditions are somewhat improved to-day. In what sense can such a life be considered physiological? Only in so far as it is a means of supplying energy in the form of food which is essential to life. A minimum of mental and physical exercise is required. All the senses are used to a minimum. A change of posture is now advised and made possible, but full advantage is seldom taken of this privilege. The workers become mere automata. Such an existence can scarcely be compatible with the physiological function of organs and it is indeed marvellous how the body can become adapted to such a life at all.

An extreme example has been given, but more and more evidence is accumulating that monotony of stimulation is an important factor in everyday life. To continue working for long periods, especially at high pressure, or under conditions of anxiety, inevitably breaks down the health of those who attempt it. The value of holidays is well appreciated and the more the holiday differs

from the normal mode of life, the more efficient is it likely to be. A holiday is not altogether a matter of rest, as at first sight would appear. Inland dwellers benefit from a visit to the seaside and *vice versa*. Town dwellers enjoy the country, but those who live in the country go for holidays to the town. The value of "a change of air" has long been appreciated by physicians and by the public alike since the days of Hippocrates.

Holidays, however, should not be prolonged except after special strain, and it will be generally agreed that the first month of holiday is always more efficient in its recuperative power than any succeeding period.

Monotony is prevented by congenial occupation. Those who find real pleasure in their work are able to work extremely hard at it without any harm accruing. Indeed, the work promotes health, provided it permits of a reasonable amount of physical activity. They are the most happy, contented, and usually the most successful amongst us, and also the most physiological. It is a noticeable fact that the most eminent men of our time are amongst the longest lived, and long life we must consider the final test of physiological living. Consider further the condition of life of that section of society, country ministers and farmers, which head our vital statistics, and we see the essential of a physiological life, lack of worry, lack of monotony, and moderate exercise.

In two classes of society monotony is extremely difficult to relieve. The unemployed, rich and poor, suffer from similar complaints. For the former, social excitements, travelling, and games may cause a temporary relief, but if not kept up often exaggerate monotonous conditions of home life. The provision of an occupation, preferably involving a reasonable amount of physical exercise, is the ideal treatment in both instances.

The provision of work which gives interest to the individual workers is one of the most difficult social and economic problems of to-day, and there can be little doubt that the general tendency for workers to eliminate competition and pride of work amongst themselves has reduced appreciably the interest in a large number of occupations. Far be it from the intention of a physiologist to attempt to solve such problems, but on purely physiological grounds, the greater introduction of interest into labour by the workers having a real share in the result of their work seems to point in the proper direction.

We do not as yet know the exact method by which monotony produces its ill effects. It is evident that it is quite different from fatigue in the ordinary sense. Mere rest in bed and plenty of sleep is not the efficient remedy it is for overwork. An analogous, if more localized condition, known as "stale-

ness," is well recognized in athletics. There is no actual fatigue, but the zest has gone and the maintenance of training becomes a mental weariness while the efficiency becomes markedly reduced. Many of the problems of the Industrial Fatigue Board are of a similar nature. It may be that there is too little variety of sensory stimuli, or that there is localized exhaustion of nerve cells responsible for the too-often repeated motor movement or mental work. The fact that a change of occupation is as beneficial as a rest, indeed often more so, suggests the former cause, as does also the fact that in the condition there is also often a considerable degree of mental languor, and that in a change of occupation the nerve cells, previously overwrought, may get some degree of rest.

There seems to be little doubt that the mental state is the most important, since if two people have a similar occupation, they are not both affected by its monotony. Interest, if such can exist in connection with it, prevents its occurrence. Interest depends on the mental state, especially on the mental outlook.

Undoubtedly a great deal can be done by studying the mental and physical make-up of the individual, and allowing him to follow his or her natural bent. Psychologists indicate how many of the apparently trivial matters of childhood may awaken interest along certain lines, and later industrial psychologists emphasize the importance of finding the occupation to which the individual is best suited.

Therapeutically, if the physical circumstance cannot be readily altered, much can be done to improve the mental outlook by teaching that content is the true philosophers' stone which can convert the lead of monotony into the gold of happiness.

CHAPTER XXXVI

PROTECTION AGAINST DISEASE

It is one of the greatest indictments against civilization that the natural defences of the body against certain classes of organisms under its influence are not fully maintained. One has only to be acquainted with life in some communities exposed to infection to realize how far we are deficient. I have in my mind as a striking example, one of the most ancient cities of the East, where the water supply comes from a well by the city, runs down the filthy streets—for there are few real gutters—to an ancient and practically stagnant walled pool. This water the inhabitants put to all the purposes for which water may be used and yet are apparently none the worse, as they must have natural immunity against water-borne disease. It must be confessed, however, that natives are quite prone to many of the common infectious diseases, although they are seldom exposed to infection. In war-time we saw clearly that even our attenuated resistance to infection could be appreciably increased by an active and open-air life. It became possible to withstand a degree of exposure almost inconceivable in peace-time, while it was found that a considerable immunity to bowel infections occurred after a few years of association with natives.

Our resistance may conveniently be divided into two categories, that by which the entrance of bacteria into the body is prevented and that by which the body defends itself against bacteria and their toxins when they have entered. These protective mechanisms must be considered physiological, as they are normally present in all animals, although their study has mostly been carried out by bacteriologists and pathologists.

Skin and Mucous Membrane.—In the first category are the skin and mucous membranes which act as a mechanical protection, for the mucous membrane of the alimentary canal is quite as much exposed to bacteria as the skin. Especially is this the case in the large intestine where bacteria are of normal occurrence and in the lower animals take an essential part in body economy as in the breaking-down of cellulose.

The protective value of the skin depends on the fact that the upper layers are tightly packed together and are impervious. In the event of injury, also,

the skin has an exceedingly rapid power of repair which is best where the circulation is good, but less rapid where it is liable to be impaired, as in the legs, a point of great practical importance. Thus, in ulcers of the leg, the circulation and process of repair are greatly improved by raising the limb. The skin may, however, become infected by way of the hair follicles and sebaceous glands, especially if subjected to abrasion, or if the general resisting power of the individual is reduced.

Should the skin protection fail, and bacteria enter the subcutaneous tissue, they are at first held up by the immigration of the **leucocytes**, which process is facilitated by increased vascularity of the part, as the result of which we have the well-known characteristics of inflammation—heat, redness, pain, and swelling. Usually, if the infection is mild, the invasion may remain local, as a papule, a boil, or carbuncle, according to its size. This is not, however, invariable, for, as in tetanus, there may be little or no local reaction, while the toxin produced in the wound may be of great consequence.

The next line of defence is the **lymph glands** which are congregations of lymphoid tissue and may be considered the home of the lymphocytes. In some diseases the effect on the lymph glands may be really more important than the local reaction, as in plague, where there is no evidence necessarily of the entrance of the bacilli, although their presence is made clearly evident in the characteristic bubo. In certain regions, normally liable to infection, the lymphoid tissue may be situated immediately under the mucous membrane as a special safeguard. The naso-pharynx is protected by the lymphoid tissue in the tonsils and neighbourhood. Clinically, these are of importance, as such adenoid tissue may become the seat of inflammation and chronic enlargement under conditions which suggest excessive demand on their function. Similarly, we have at the lower end of the small intestine aggregations of lymphoid tissue known as Peyer's patches, which, according to Barclay Smith, may be looked upon as protecting the small intestine from the invasions of bacteria from the large colon. These too, however, may be overcome by bacteria and their toxins, as they are in typhoid fever, in which the patches become the main seat of the disease.

The upper part of the alimentary canal is, apparently, protected by the digestive secretions, and this no doubt accounts for the comparative immunity from infection in this region, apart from that associated with gross lesions. It has been shown experimentally (Cornwall) that injections of bacteria which in animals produce no marked effects if introduced into the stomach, bring about severe infections if introduced into the ileum. There is, however, a distinct

limit to the protection, as may be well adduced from the tenets of public health. Thus, for example, water which contains bacillus coli (this bacterium being used as an indication of possible infection), in ·5 c.c. would be considered unsafe, while if the organism is not readily demonstrable in less than 10 c.c. of water this might be considered safe, if otherwise suitable. Obviously, the underlying principle of these considerations is the concentration of bacteria which can normally be dealt with and the immunity of natives to bowel complaints may be due to the benefits conferred by simple diet which does not overtax their digestive mechanisms. All the main ducts of glands which open into the alimentary canal are well supplied with digestive secretions, although we know that occasionally these ducts may become infected, causing inflammation in such as the bile passages or the pancreas, the latter more rarely no doubt in virtue of the digestive properties of its juice.

Kidney.—Once bacteria have gained access to the blood-stream there is good evidence, such as that of Kidd and of Chalmers Watson, that they may become eliminated by the kidney. There can be little doubt that, if proper culture media are used, the occurrence of a sterile urine is much less common than has been usually supposed. It is considered that should the kidney become overstrained in this respect, the organ itself may become attacked and become the seat of disease, which will vary with the bacteria concerned. The existence of such a mechanism is supported by the fact that the kidney may become the seat of blood-borne disease which does not necessarily exist in any other part of the body.

Reticulo-endothelial System.—More recently it has been shown that the Kupffer cells of the reticulo-endothelial system, especially in the liver (see bile formation), have the power of ingesting bacteria which are excreted in the bile, a fact possibly of importance in relation to infection of the biliary passages.

Immune Bodies and Lysins.—These substances are produced in the blood to operate against bacteria which they kill by a process of dissolving or lysis. It is, however, interesting to note (Muir) that these substances are not themselves capable of destroying bacteria, but act as sensitizers in that they make it possible for the substance known as *complement or alexin,* normally produced in the serum, to attack the bacteria. The immune bodies are, however, specific, that is, they can deal only with special classes of bacteria or special antigens. The sensitization is developed also towards foreign blood corpuscles (should they be injected into an animal), and this fact is of considerable importance, for such corpuscles may be utilized as a test for complement in an unknown serum. If the complement has been fixed it is no longer capable of causing

the lysis of sensitized corpuscles, as in normal serum. Applications of these principles are a basis of the Wassermann test in syphilis. Thus, if an unknown serum is added to a syphilitic antigen plus complement and when added to the sensitized corpuscles it is found to have its complement fixed, this is considered to be evidence that the unknown serum contains an immune body which has been intended as a protection against this particular disease.

Opsonins.—In many respects these substances are like immune bodies, but they are different in that they can act in the absence of complement. They are specially important in that they lead to the phagocytosis or destruction of the bacteria by the leucocytes, which can be seen to ingest the bacteria and apparently to digest them. In the absence of the opsonin the phagocytes cannot attack the bacteria and it will be obvious that their presence plays a most important part in rendering the body resistant to bacterial invasion, for its absence would be of grave significance in disease. Reference has already been made to the fact that an insignificant leucocytosis in conditions where a large one is expected, indicates that the bacteria are obtaining the mastery. Endeavours have been made to estimate the body resistance by the number of bacteria ingested by the phagocytes under suitable conditions in vitro. This estimation of the "opsonic index," as it is called, has not, however, been generally useful, largely owing to the difficulty of obtaining standards. What exactly causes the opsonins to be formed is yet unknown, nor is it yet understood by what mechanisms enormous numbers of leucocytes are caused to assemble in diseased or injured areas, although as the word chemiotaxis indicates, we suspect an attraction of a chemical nature.

Antitoxins.—At the same time as immune bodies and opsonins are dealing with the bacteria the toxins of the latter are being neutralized by antitoxins and rendered innocuous. In some instances, as in diphtheria and tetanus, the toxins produced are extremely powerful and produce dire results. Fortunately these organisms, especially the former, also cause powerful antitoxins to be formed, not only in man but in other animals. Thus it is possible to inject the toxin made from killed bacteria into an animal (such as the horse) and subsequently withdraw some of the blood of the animal to obtain a serum which is rich in antitoxin, and which may be injected into man to combat the disease. Not only are the toxins neutralized, but the bacterial growth itself is inhibited and so the antitoxin may be utilized as a prophylactic.

The immunity thus conferred is known as *passive immunity,* as the tissues of the individual are rendered immune although they play no part in the production of immunity. Where, however, the antitoxin, together with the lysins

and opsonins are formed as a result of the reaction of the individual, the term *active immunity* is used. Thus, in diphtheria antitoxin, there is active immunity produced in the horse. Such immunity takes more time to produce, but lasts appreciably longer and is part of the natural cure of bacterial disease.

It is an important point that for the production of an active immunity it may not be necessary to inject living bacteria, since the toxins of bacteria, grown and killed in vitro, bring it about, and it is thus possible to control the amount of toxin injected.

We see, then, the physiological principles on which vaccination and inoculations are based. The vaccines ingested are dead or attenuated bacteria and their toxins and are intended to set up an active immunity, either as a prophylactic, as in typhoid or small-pox, or therapeutically where it is considered that an infection, possibly because it is shut off by the local reaction it produces, does not produce a general reaction. It will be obvious that, therapeutically, it is important, in view of the specificity of anti-substances, that the bacteria or toxins should be of the same variety as those concerned in the infection. Where there is doubt of this, autogenous vaccines, i.e. vaccines produced from cultures of bacteria taken from the actual patient, are necessary, but stock vaccines of a more "blunderbuss" type are commonly utilized.

It must be remembered that the injection of vaccine does throw some strain on the reserves of the patient, and if the response is not good may actually do harm. Harm may be indicated by excessive local, i.e. at the site of the injection, focal, i.e. at the site of the lesion, or general reaction, any of which indicate a reduction of the dose or a lengthening of the interval between the doses. These reactions indicate, especially the local and focal, that temporarily the bacteria have got the upper hand, and may extend the lesion. Hence, the imperative necessity of their avoidance.

There is as emphasized by Philip little doubt that failure in vaccine therapy has in a large measure been due to neglect of this precaution and to the routine of giving standard doses at stated intervals irrespective of the response of the patient.

These local reactions have been utilized for diagnostic purposes. Thus, in von Pirquet's test for tuberculosis, tuberculin is applied to the scarified skin. The application of Moro's Tuberculin Ointment to the skin may be similarly used, though, in the latter instance, it may be first necessary to increase absorbability by the application of a fomentation. In the Schick test, too, in which a little diphtheria toxin is introduced intradermically, use is made of a

similar reaction in determining whether or not individuals exposed to infection should be given prophylactic doses of diphtheria antitoxin.

Finally, when the body gets the upper hand, bacteria may settle down in the tissue and give rise to very little general reaction. Locally, there is the formation of granulation tissue, of which the tuberculous nodule is a well-known example, or the formation of fibrous barriers. In the abdomen, the localization of infection is facilitated by adhesions of peritoneum and the coagulation of the lymph. In this way an abscess may become completely shut off, and may finally become absorbed. Unfortunately, it is not possible to predict the extent to which the individual may react, and surgical evacuation of the abscess is a much more certain method of bringing about recovery. When the bacteria become enclosed in granulation or fibrous tissue they tend to lose their vitality and die. A fibrous nodule only remains. Occasionally, the fibrous tissue is further assisted by the deposition of lime salts.

Unfortunately, too, there occur instances of what Mackie calls "a non-sterilizing immunity," as exemplified by the convalescent carrier who, although he may himself be immune from acute infection, may pass on a virulent organism to another person. The treatment of such a carrier, e.g. diphtheria in the nasal passages, typhoid bacilli in the intestines or gall bladder, is often extremely difficult, even if the carrier himself can be found, a matter often of no little difficulty, as the carriers may be normal people.

Precipitins and Agglutinins.—These substances are found in serum on the injection of antigen and appear to be of the nature of anti-substances, although their exact significance in relation to immunity is uncertain. They are, however, important clinically in diagnostic methods.

A precipitin is so called because it causes a precipitate to be formed if added to the serum similar to that injected into an animal to cause its formation. Thus, if human blood is injected into a rabbit, a precipitin will be formed in the rabbit's serum which will cause a precipitate with human blood. This is made use of medico-legally to differentiate between human and other blood, the unknown blood being added to the previously obtained serum of an immunized animal.

Agglutinins have the peculiar property of causing clumping and sedimentation of bacteria where the latter are similar to those which have previously been injected into the animal. Thus it may be utilized for differentiating bacteria, and is made use of in the Widal Reaction. When positive in typhoid fever, the serum of the patient in appropriate dilution agglutinates the bacillus typhosus.

Body Temperature, Oxygen Supply, General Metabolism

The fact that a chilling of the body is liable to lead to infection is well known, and has been referred to in relation to the body temperature (page 286). Unless the latter is kept up invading organisms are likely to get the upper hand. The effect of cold seems to be that local metabolism plays a distinct part in the protection of the tissues. This is further seen by other factors which affect metabolism. Thus, if the oxygen supply is diminished, e.g. in venous congestion or anæmia, there is a special liability to local infection often difficult to clear up. If the fuel supply for the maintenance of local fire, as it were, is difficult, a similar state of affairs is seen, as in diabetes where boils, gangrene, and tuberculosis are common complications. In myxœdema, prior to thyroid treatment, the liability to death from intercurrent infection was well known. Here metabolism is extremely slow. Analogous, too, is the liability of a starved person to infection.

How this reduced local metabolism affects resistance is not clear. Possibly the production of antibodies and vascular reaction are reduced in such circumstances.

Open Air and Exercise

The fact that individuals who live open air lives are appreciably less liable to catarrhal affections of the respiratory tract was well proved in war time. This is explained by the fact that exercise by increasing respiration increases the evaporation from the respiratory tract and in order to maintain the normal surface moisture and temperature a considerable local circulation has to be kept up. If this protective circulation is not required as in a sedentary worker especially in a humid atmosphere the mucous membranes are more liable to infection.

Alcohol and Salicylates

The belief that alcohol is of value in cutting short or protecting against such catarrhal infections is too strong to be dispelled on negative scientific grounds. It does not appear to have been suggested that the benefit may be the result of similar hyperæmia of the respiratory tract during the excretion of the alcohol. That salicylates bring about an increased circulation through the pharyngeal mucous membranes is certain; indeed in some individuals this may be intensely disagreeable.

CHAPTER XXXVII

THE SKIN

Were it necessary to obtain evidence of the statement that a true physician is born not made, it could be well seen in the different amounts of information which two doctors (apparently equally trained) could obtain from a glance at the face of a patient. For the general practitioner, the more rapidly the information can be obtained the better. A mere look at the face plays no inconsiderable part in his everyday diagnosis. The expression, the pupils, and teeth, each have a special significance, but that of the skin and subcutaneous tissue is more general.

The skin is designed as a protective covering, at the same time having a function in relation to the regulation of body temperature and as an organ of excretion. It presents certain normal characteristics which in virtue of these functions vary noticeably in pathological states.

Colour.—The colour of the skin of the so-called white races is dependent on the blood which flows through it or, to be more accurate, on the amount of hæmoglobin in the corpuscles occupying the superficial blood-vessels. Let the blood be removed or the percentage of hæmoglobin much reduced and the skin becomes pale. Clinically, all degrees of such pallor are seen. For in conditions of blood loss, the vaso-motor system conserves the existing blood for the more important organs by reducing that flowing to the skin. Skin pallor, then, may be an indication of hæmorrhage, and this may be extremely valuable in cases of internal or concealed hæmorrhage. It may, for example, indicate the rupture of a vessel in the lung or alimentary canal, an unsuspected aneurysm or a ruptured extra-uterine pregnancy. Taken together with the previous appearance of the patient, it may be of the utmost importance, as the life of the individual may depend on immediate surgical measures. The pallor of vaso-motor disturbance commonly associated with fainting is of a similar nature, but in this instance the blood has accumulated in the splanchnic area. The pallor of death is, similarly, due to constriction of the skin vessels as the result of the stimulation caused by the fall of arterial pressure. Subsequently, when the capillaries and arterioles lose their tone, they are filled with blood from the venous side, and there then results a bluish appearance.

Pallor of a more chronic nature may result from frequent loss of blood, as in hæmorrhoids, from which large quantities of blood may be lost without the knowledge of the patient. More commonly such pallor is due to a reduction of the percentage hæmoglobin in the blood, as in anæmia. The skin indeed is pale simply for the same reason that an Oliver's hæmoglobinometer would give a low reading; in a given area of skin, just as in a given quality of blood, there is a reduced amount of hæmoglobin. The pallor seen in many illnesses is commonly due to anæmia caused by the bacterial invasion or toxins and other conditions present often lead to characteristic shades such as the yellow-green of the anæmias, or the more dead waxy white of nephritis, which is exaggerated by any œdema.

In the same way the blood supply of the skin may be interfered with mechanically as in embolism, or the interference may be in the skin itself as in œdema, in which the pressure of the fluid in the subcutaneous tissues interferes with the skin circulation and gives to it its pearly pallor. Thus is produced "the large body" of chronic tubular nephritis, and it has to be remembered that such tissue is, because of its scanty blood supply, less capable of withstanding infection.

A heightening of the colour is caused by corresponding processes and is due to an excessive amount of blood or hæmoglobin. The flushed skin seen in exercise, and fever, indicates the attempt of the body to get rid of heat. Why, however, certain areas become flushed is difficult to explain. The localization of the blush of self-consciousness or the more local malar flush in tuberculosis, are as yet difficult of explanation, just as the fact that atropine dilates especially the vessels of the cheek.

The whole question of the distribution of the rash in the exanthemata provides an interesting physiological problem. In the formation of localized spots in these conditions it may well be considered that only those capillary areas which chance to be open at the time of the distribution of the infection are the site of the localized dilatation of vessels or papule formation or hæmorrhage. The fact clearly shown by Krogh that only a proportion of the capillaries are in constant use when the body is at rest has already been alluded to, and this together with the finding by Waterston and Herring that the hot and cold spots of the skin vary would tend to support this explanation. In the skin certain capillary loops are permanently open while others open and close (Hemingway). An explanation of the circumoral pallor in scarlet fever may similarly be explained by the fact that the nausea so characteristic of the condition reduces the movement of the mouth area, as food is not desired and the capillaries of

this region are for the most part closed when toxins causing the rash are thrown out. The region of the mouth is that part of the face which receives most movement, and no doubt takes every opportunity to rest. In measles, on the other hand, appetite is maintained, and the movement of this region is increased by the associated irritation of the upper air passages. Possibly rash distribution in general could be explained along similar lines, though the details are not clear.

Local stimulation, by wind and sun, will bring about a high-coloured complexion, and so will alcohol from its dilator effect on the skin capillaries. Dyspepsia also produces an unfortunate similarity to the latter drug. Here we may consider that the capillary dilator bodies, such as histamine, are absorbed in the alimentary canal.

The quality of the blood may cause the skin to be highly coloured as in polycythæmia, where the number of red corpuscles is in excess of the normal. Should the blood contain abnormal coloured substances they will be evident in the skin, as bile in jaundice, melanin in Addison's disease, methemoglobinæmia, and chronic poisoning with dyes or metals such as silver and arsenic. Mere stagnation of normal blood in the skin will allow the blood to lose more of its oxygen and become more venous, making the skin of a purple or cyanotic colour. This may be due to a protective closure of the superficial arterioles and capillaries against heat loss under external cold, or general stagnation from a faulty circulation so characteristic of impairment of the right ventricle. Local colour changes due to circulatory changes may occur as in nævus, or birth mark, in ecchymosis, or rupture of the skin vessels, as in bruising.

General State of the Skin.—The state of the normal skin is familiar to all and depends on a variety of conditions of which the most important are the blood and nerve supply, together with secretory and endocrine activity, all of which are necessary if the skin is to perform its functions adequately. Obviously if the blood supply is cut off the skin will become dry and its nutrition impaired. In gangrene the skin becomes involved with the rest of the part to which the blood supply is reduced and the ease with which varicose ulcers in the leg heal as soon as the circulation to the part improves by raising the limb indicates the importance of blood supply in this relation. Similarly, heavy individuals who have to lie in bed for long periods are specially apt to develop sores if not attended to.

The trophic influence of the nervous system is important in relation to the skin as in relation to the muscle and in chronic nervous disease, and especially in injury to the spinal cord, the prevention of bed sores is a test of good

nursing. The water bed, air cushions, the hardening of the skin by applications and the frequent change of position if the lesion permits, are the usual preventive procedures adopted.

The thyroid is seen to play an important part in relation to the general nutrition of the skin. In myxœdema, in which the internal excretion of this gland is insufficient, the skin is extremely dry and brittle, and the hairs tend to fall out. Still more striking, is the somewhat gelatinoid degeneration of the subcutaneous tissues which gives a puffy appearance and from which the disease takes its name. This condition of the skin has, however, to be clearly distinguished from œdema (page 277) and mere adiposity. In the former, the tenseness and the pitting on pressure are as characteristic as the elasticity in myxœdema. Adiposity is to be recognized by its distribution and the normality of the skin colouring. Individuals suffering from this condition frequently require considerable persuasion before they believe that their complaint is such a simple one, as an increase in girth, for example, may be the only feature noticed. I have known a patient imagine she had an abdominal tumour when in reality the distance of the skin from the abdominal muscles, which can be felt if made to contract, and the deep umbilicus, showed clearly that the increase of girth was really subcutaneous (and no doubt also omental fat).

The secretion of sweat, which we have seen plays a large part in the regulation of body temperature, gives the body surface its characteristic moist feeling. The secretion is, however, quite independent of temperature, as is seen in the cold sweat of fear. The latter must be differentiated from the cold sweat which is experienced after excessive sweating, often due to the administration of drugs such as salicylates and which makes it important that when such drugs are given, care must be taken to avoid excessive chilling of the body in the early hours of the morning when the action of the drug has worn off and the sweat is still upon the skin. The same applies to the taking of toddy at bedtime. Mention might perhaps be made of the old wives' cure of sweating out an incipient cold by taking, warmly clad, a brisk walk. The beneficial effects of exercise, provided it is not excessive, no doubt depend on the general dilatation of the vessels which results, and invigoration of the circulation, especially of the respiratory tract.

Whether the skin is of any importance as an excretory organ in the normal person is very difficult to decide. It is certainly capable of excreting substances such as urea normally excreted by the kidney, but these may simply be carried out by the sweat necessary for heat loss. On the other hand, it is evident that drugs are definitely excreted by the skin, such as bromides and

iodides, which may cause irritation during the excretion. Elimination by the skin is important in the case of alcohol. An individual may be quite sober in a warm room as the rate of the excretion of alcohol keeps pace with the absorption from the intestine. On going out into a chilly night the skin capillaries at once close down to conserve heat and the excretion of the alcohol is much reduced. The concentration in the blood increases as the absorption continues and the individual becomes narcotized. The large excretion by the skin no doubt accounts for the fact that in hot countries large quantities of alcohol may be ingested with impunity so far as the nervous system is concerned. Although, however, the arterial concentration does not become high, the concentration in the portal system through which the alcohol is absorbed may be very great and sooner or later affects the liver to bring about those signs and symptoms associated typically with the "climate of India."

In renal disease the excretion by the skin becomes more important. Mackenzie used to relate an instance of a lady seriously ill whom he upbraided for powdering her face, only to find that the appearance was caused by the excretion of salts from the abnormally active skin. Advantage is taken of skin secretion by the physician in the treating of kidney disease in which the skin is kept active by special measures. These have already been dealt with.

A large number of skin diseases are met with, many being due to various forms of irritation and infection which may affect it from the surface or be brought to it from the blood. Under different stimuli the skin reacts in different ways. For example, the eruption may be moist or dry, pustular, vesicular, or nodular and so on. Again, the skin lesion may be extremely sensitive, painless or even anæsthetic. These matters cannot be discussed in any detail, but there is a great deal of interesting physiological work to be done in relation to skin disorders, especially with reference to sensation and secretion (especially sweat).

CHAPTER XXXVIII

THE AUTONOMIC NERVOUS SYSTEM

THE SYMPATHETIC-PARASYMPATHETIC BALANCE

In various chapters we have seen examples of this balance, but with a broader outlook in physiology the time has come when we can no longer consider the body as a collection of units, but as an integrated whole. This is true not only in health but also in disease. The chief means by which the integration is brought about is by the maintenance of the sympathetic-parasympathetic balance.

In considering the heart rate we have noted the balance between the sympathetic and vagus nerves. It is now becoming more clearly established that a similar balance not only exists in a great variety of individual organs but also between large groups of organs associated with similar functions. The vagus is but an example of the group of nerves arising from the central nervous system which we know as the *cranio-sacral autonomic or parasympathetic*. The group includes the third nerve which constricts the pupil, the chorda tympani (responsible for salivary secretion), together with the sacral outflow which gives rise to the *Nervi erigentes* or pelvic nerves supplying the pelvic organs. The term *sympathetic* is now restricted to those fibres which issue from the spinal cord between the first thoracic and second lumbar segments, and their associated ganglia and connections. The sympathetic and the parasympathetic, together with the *enterosympathetic*, which is the intimate nervous supply of the intestine, make up, according to the Cambridge nomenclature, *the autonomic nerve system.*

The functions of the sympathetic and parasympathetic are essentially different and opposed and are probably best realized in the changes which occur in that physiological adaptation which occurs in the life of every animal, namely, exercise. The sympathetic is essentially concerned and brought into activity under circumstances in which the animal is called upon to do increased external work. The parasympathetic, on the other hand, is most active during conditions of bodily rest, although it also assists in preventing excessive damage from over-action of the sympathetic.

When muscular exercise takes place every effort is made to provide the muscle with additional supplies of fuel and oxygen. The circulation, as we have seen, becomes appreciably more rapid from a variety of causes and clinically this is evident in the increased heart rate. As sufficient oxygen is not stored in the body respiration becomes more efficient, a greater lung area being brought into use and a renewal of alveolar air more frequent. If the exercise is severe or is associated with mental activity the pupils dilate and in the lower animals the hair bristles.

The additional supply of blood to the muscles is only made possible by the shutting down of activity in other regions, for the amount of blood available is limited. All activity associated with digestion is then reduced or entirely stopped. This is made possible by the fact that adequate fuel is stored in the body as glycogen. In this form it is readily available for transformation into glucose. Less immediately available stores exist as fat. The intestinal or splanchnic area contains a large proportion of the blood, and this so-called venous reservoir is made use of in maintaining a functional balance.

We can, therefore, understand why in the case of the circulation in general the sympathetic is associated with activity or katabolism, and the parasympathetic with anabolism, yet their functions are reversed in the case of the alimentary canal. We may, however, look upon the processes of digestion and assimilation as anabolic or building-up processes so far as the body as a whole is concerned. The parasympathetic is the motor supply to the alimentary canal, and in the main controls the digestive secretions. The action of the sympathetic, on the other hand, causes closure of the sphincters, which prevents the passage of food from one section of the alimentary canal to the other, and if the action of adrenaline can be taken as an indication, inhibits the general intestinal movements.

There is evidence that the balance may not be exactly of the nature described, for it has been shown by Sharpey-Schafer, and also McSwiney, that animals with the vagi cut survive in an apparently normal way.

It is clear, then, that this balance is not essential to life. The stomach, for example, will empty without the action of the vagus, but such animals are in confinement and cannot be said to have lived normal lives. It is, therefore, more correct to consider this balance as associated with a more active physical life only. Of this there is considerable experimental evidence—by McSwiney in relation to the alimentary canal and by the author in relation to circulation and respiration. The former suggests that the action of the vagus is regulative rather than essentially motor. Since it may be shown that normally in the

young adult the vagus is constantly active and its action on the various organs is that described, the general conception of the balance seems justifiable.

The appreciation of the group balance makes it clearly evident that periods of excessive external activity should alternate with periods of rest, and this is common amongst wild animals. The disinclination for activity after a meal is common experience, and the disadvantages of disregarding it can be made evident by examination of the stomach by radiological means or a study of its contents, as has recently been done at Guy's Hospital and elsewhere. If severe exercise be taken it has been shown that there is considerable delay in the emptying of the stomach. It is interesting to note that this delay is enhanced if the individual has not the opportunity of conversation during the exercise. It may be presumed that the sympathetic stimulation and reduction of vagal tone which take place to facilitate the supply of fuel and oxygen to the muscles at the same time prolongs the evacuation of the stomach which is normally augmented by the vagus. The parasympathetic is also largely responsible for the general digestive secretions such as the salivary, gastric and pancreatic, and in consequence of diminished parasympathetic activity will also be reduced. This will be further emphasized in severe exercise by increased water loss in the sweat.

In ordinary life it is generally accepted that those who "run and snatch" their lunch suffer from indigestion as a result. It must be remembered, too, that different mental states may act similarly. It has already been noted that the heart rate is already increased by the anticipation of exercise and this may be taken as indicative of an alteration in the sympathetic-parasympathetic balance. When we consider, too, the enormous influence which the appreciation of food plays in digestion, it is not far to seek why individuals who habitually continue work or mental exertion at meal-times suffer from gastric complaints.

The same principle, however, it will appear may be carried still further into disease if the sympathetic-parasympathetic balance is likewise affected. Digestive troubles are notorious in the anæmias in which the increased sympathetic action has already been noted as an adaptation of the circulation to make up for the blood deficiency. Similarly in acute disease the lessened power of digestion is well recognized and no doubt depends on like reasons, although in such conditions there is in addition diminished secretion from excessive water loss, as in exercise, as well as the diminished vagal activity. In pernicious anæmia in particular, it is well known that treatment with arsenic causes stomach trouble, and the more easily digested foods are given in fevers.

The possible effects of nicotine on the balance have already been referred

to in relation to the heart. There is no reason why, as more recently Patterson has emphasized, paralysis of the sympathetic or parasympathetic synapses should not affect the nervous control of the alimentary canal. The mode of action of various toxæmias in respect to this balance and their influence not only on the circulation and nervous system but also on digestion is indicated by modern work which in the near future ought to throw a considerable light on the subject. It is possible, for example, that the substances absorbed in constipation and intestinal toxæmia may affect the balance and thus account for indigestion which commonly accompanies these conditions.

The Protective Function of the Vagus.—While, as has been said, the parasympathetic is on the negative side of the balance so far as exercise is concerned, it does play a very definite part in preventing over-activity of the sympathetic. Should the pressure in the aorta become too high as the result of increased cardiac action, together with increased resistance from muscular contraction, impulses pass up from the aorta and left heart by way of the depressor fibres of the vagus (or sometimes a separate depressor nerve) to act upon the vagus and vaso-motor centres, bringing about a slowing of the heart and a peripheral dilatation respectively. An analogous state is produced, too, experimentally if a large dose of adrenaline is injected into the vein of an animal. An excessive rise in blood pressure is prevented by slowing of the heart, not only by the rise of pressure itself, but also by action on the vagus centrally. The extent to which vagus tone is developed depends on the activities of the individual animal. Pet animals have appreciably less tone than field animals, and in the case of human beings, old persons have considerably less than young ones, while it has been shown that in men who take much physical exercise, the pulse is low. Especially is this true of runners. But even after acute experiments this increased parasympathetic tone is found. It may be produced in cats (McDowall). After slight asphyxia it persists for some time after the usual asphyxial signs have passed off. Similarly, after running up stairs, the acceleration of the pulse is followed by an abnormal slowing. Nor is this increased parasympathetic tone confined to the circulation. After exercise, we are familiar with the occurrence of increased peristalsis, while it has been found (Lawrence) that exercise causes a secretion of insulin, which we know to be controlled by the parasympathetic. These facts are as yet unexplained, but it seems probable that the parasympathetic stimulation which occurs after exercise will be related to the result of the utilization or mobilization of the alkali which occurs during the exercise. On general grounds it may also be considered that animals which are extremely active become automatically

endowed with unusually active digestions and thus the digestive power is adapted to the energy requirements of the individual.

The sympathetic-parasympathetic balance is also of great value to the individual because of the greater sensitivity it gives to nervous mechanisms and the reduction, as it were, of inertia. The response to the requirements of the body is thus rendered immediate, and may even anticipate the requirement.

It will be seen, however, that the adaptation to external circumstance may be brought about by the action of hormones or chemical messengers, some of which appear to come in on the sympathetic side of the balance and some on the parasympathetic.

Strictly speaking, the carbon dioxide, which is a product of combustion in all tissues, may be considered not only as an excretion, but also as a hormone, and it has the characteristics of such substances. It is, for example, readily diffusible, specific in its action on the circulation and respiration, and produces no antibodies. The results produced by small amounts of carbon dioxide on the circulation are exactly those produced by sympathetic stimulation.

Adrenaline.—Of special interest in this connection, also, is the action of the extract of the medulla of the suprarenal known as adrenaline. Its actions are so completely identical with stimulation of the sympathetic that the probability of its being thrown into the circulation in conditions of emergency for the purpose of enhancing the action of the sympathetic and of carbon dioxide is getting beyond the realm of doubt. This is supported by a study of the development of the suprarenal medulla which is formed from that part of the primitive neural ridge which gives rise to the sympathetic. It is true, as pointed out by Swale Vincent, that there is a paucity of direct and conclusive evidence as to the passage into the circulation of adrenaline to an extent which would cause a rise of arterial pressure. It must be remembered, however, that under normal conditions adrenaline will presumably *not* act independently but in conjunction with the sympathetic and carbon dioxide. The ion concentration of the medium in which the adrenaline is present has also opened up new ideas. On the whole, then, it is justifiable (as concluded by Sharpey-Schafer) to consider that the evidence is fairly satisfactory, and that there is a normal secretion of adrenaline into the blood, especially under conditions of mental or physical stress.

The effect of adrenaline, then, so far as the autonomic balance is concerned, is similar to that of atropine (see below), although it affects the opposite side of the balance. Adrenaline is now extensively used in the relief of asthma, but it has not yet been taken up enthusiastically for its heart action. Injected

intravenously it is, in virtue of its action on the sympathetic, the most powerful cardiac stimulant known. It increases both the rate and force of the heart and is extensively used for this purpose in experimental work. There seems to be little doubt that the lack of appreciation in clinical work is due to several factors. When it was originally introduced solutions of adrenaline were available only, and varied greatly in strength, as they deteriorate rapidly in solution in virtue of the ease with which they become oxidized. Subcutaneous injection is slow in its effect. On the other hand, when injected intravenously overdosing occurred, and it can be readily demonstrated experimentally that overdosing with adrenaline in this way can lead to a degree of sympathetic exhaustion which may be fatal from its effect not only on the heart, but also on the blood-vessels. Now, however, that solid synthetic adrenaline is available from which solutions of accurate strength can readily be prepared, there is undoubtedly a large field for the investigation of the proper methods of administration of the drug in the cardiac emergencies, as its efficiency is undoubted.

Histamine.—The importance of this drug lies in the fact that it represents a group of amines which are derived from the breaking-down of protein. Histamine is formed from the decarboxylation of histamine, which is a normal product of protein digestion. Similar, if not identical substances are also produced normally by the growth of bacillus coli. It is evident, then, that histamine is a normal constituent of the intestine and may presumably be absorbed to some extent. Experimentally, the injection of the substance in large quantities may cause shock from capillary dilation, but the author has shown that there is a compensating mechanism by which the cardiac output is increased and the peripheral resistance raised by arterial constriction, as in hæmorrhage. Histamine undoubtedly stimulates the sympathetic side of the balance. There is indeed evidence, such as that of Kellaway and Cowell and of Dale and Burn, that adrenaline may be secreted to enhance the sympathetic action and antagonize the histamine. In addition to the reflex action on the arteries, histamine has a direct action on all smooth muscle, and this, together with the reflex action, makes it evident that the possibility of the absorption of such substances from the intestine may bring about arterial hypertension in man is one which at least requires a great deal of consideration.

Atropine.—By far the most important drug which affects the sympathetic-parasympathetic balance is atropine, which paralyses the endings of the parasympathetic. The use of preparations of belladonna, indeed, for this purpose, preceded our knowledge as to the mechanism of their action. By paralysing the parasympathetic nerve endings in the third nerve the pupil is dilated from

over-action of the other side of the balance, and use is made of this fact if it is desired to examine the fundus of the eye or to keep the iris out of a corneal wound. Atropine is also extensively used to diminish secretion during operations, especially on the upper air passages. There can be no doubt that in catarrhal conditions which result from irritant conditions of the bronchi, whether they be due to gas or infection, and where the patient is liable to suffocation from excessive secretion and the associated spasm, atropine is most strongly indicated. As all glandular secretions are affected, it may also be of value in sweating or to reduce the secretion of milk and in such instances local application is quite efficient.

Reference has already been made to the use of atropine to reduce the action of the vagus on the heart, which is exaggerated in the first stage of chloroform anæsthesia. In this respect it must be remembered that individuals of athletic habit are more likely to have greater vagal tone than others. As the parasympathetic is the motor supply of the alimentary canal in general, atropine is indicated in a large variety of intestinal spasms or colics where morphine is considered unnecessary. The same may be said of the use of atropine in asthma. The motor nerve to the bronchi is, as shown by Brodie and Dixon, the vagus, and the sympathetic brings about dilation, although the actual pathways have not yet been traced. When the bronchial muscles go into spasm they may be obviously dilated by paralysing the vagus with atropine or by stimulation of the sympathetic with adrenaline. Experimentally, atropine is much the more efficient and its action more prolonged, but the excessive dryness of the mouth, after atropine, is intensely disagreeable, while adrenaline usually acts long enough to relieve the spasm. Stramonium, which is a common ingredient of asthma smoking mixtures, has a similar action to atropine, but on general principles it is doubtful whether such inhalation does not itself irritate the mucous membrane and make it more sensitive. There is no reason why pituitary extract should be of any value in asthma, as it constricts the bronchi. Belladonna is often used in cases of incontinence of urine in children and no doubt acts by reducing the normal tendency of the bladder to empty itself automatically when it is but partially filled. For similar reasons it is used in vesical spasm from any cause. It should perhaps be noted that some rare individuals suffer from toxic symptoms from small doses, so that large doses should not be administered without previous knowledge of the patient.

Pilocarpine.—Pilocarpine by stimulating the endings of the parasympathetic has an action directly opposed to atropine. In view, then, of its action on the heart its use is obviously limited. By its action all glandular secretions

are increased and because of its stimulating action on the sweat glands preparations of jaborandi are given to activate the skin in kidney disease (see page 281). Probably, however, its most common use is by local instillation to constrict the pupil in order to facilitate absorption by way of the filtration angle of the anterior chamber of the eye in cases of glaucoma.

Nicotine.—The absorption of nicotine from tobacco may produce a large variety of effects for, as shown by Langley and Anderson, it paralyses the synapses in the autonomic nervous system. Its effect on the heart has already been referred to, and it has been seen that although both the sympathetic and parasympathetic are paralysed, as the normal balance is in favour of the vagus, cardiac acceleration is produced. Its effect, however, will depend largely on the actual balance in the individual. It will be evident from what has been said in relation to vagus tone that young persons, especially athletes, are more liable to be affected than the old or sedentary. The general effect of nicotine is to limit the activities of both sides of the autonomic balance so that the individual, especially as regards his circulation, is less capable of adapting himself to conditions of physical stress. This is generally admitted in athletics where smoking is taboo. The possible effect of the nicotine on the alimentary canal has just been referred to above.

In concluding any consideration of the functions of the autonomic nervous system, one is reminded of the remark of a "philosophic physiologist" (quoted by Bayliss from Bernard) that "nature thought it prudent to remove these important phenomena from the caprice of an ignorant will." In the light of our further knowledge we are also driven to deplore that civilization brings in its wake conditions with which even our delicate automatic mechanisms were never designed to deal. We look forward to the time when, with a fuller physiological knowledge, we shall lead our fellow-creatures to more physiological modes of life.

CHAPTER XXXIX

THE BALANCE OF THE ENDOCRINE ORGANS

Probably no branch of medicine suffers more from hypotheses than does endocrinology. The rapidity with which the results of the preliminary experiments of physiologists have been applied in therapeutics offers a striking contrast to the slowness of application of other more accurately known facts. Claims are often made for organo-therapy which are quite unjustified. While glandular extracts may be of value in a large variety of instances, so may tincture of cardamoms administered with due ceremony! Early interest in the ductless glands was due in part to the claims of Brown-Séquard to have rejuvenated himself by extracts of testis.

At the same time a wealth of detailed evidence has been collected which is more coherent than used to be thought. Various attempts have been made (e.g. Eppinger, Hess) to correlate this evidence. This has, however, been severely criticized, especially by Swale Vincent. He points out that much of this theory is unsupported by evidence good enough to warrant such hypotheses. At the same time it will be agreed that many facts have been demonstrated (especially in the last few years) in this field of work, and definite broad principles acceptable on general biological grounds appear to be emerging.

One of the outstanding features of the animal body is its power of adaptation, especially to exercise and use. Adaptation can be seen in every organ of whose function we have any clear conception. We are not surprised to find that the arrangement of the ductless glands provides for the body as a whole a similar adaptation. Alluding to the sympathetic-parasympathetic balance, we may divide the endocrine glands into two groups, related to external activity and rest respectively. The activity side of the balance is closely related to the sympathetic.

Activity	*Rest*
Pituitary	
Thyroid	Pancreas
Suprarenal medulla	Suprarenal cortex
Thymus	

The pituitary body (anterior lobe), as we have seen in the chapter on "Growth," is specially related to the structural adaptation of the body to its physical requirements, for if the bones are of sufficient size the muscles will readily adapt themselves to the requirements of the individual within his lifetime. This adaptation is obviously of a hereditary nature and the result of the experiences of past generations. The posterior lobe of the pituitary, on the other hand, is concerned with the adaptation of the body to the processes necessary in the continuation of the species and is dealt with below. These two functions considered together may well be taken as the most important in the survival of a particular species.

At birth, then, the animal is endowed with certain physical adaptations. Given these, the next most important mechanism to the body as a whole in relation to its environment is the rate of metabolism which is controlled by the thyroid. Here the activity may be influenced normally within the lifetime of the individual and, as noted on page 202, he can adapt himself to lives of varying intensity. Thus we have one man leading a slow sluggish life with a low metabolic rate, and a large number of intermediate grades, until we pass to the true myxœdema. On the other hand, the same individual might under different circumstances lead a very strained and emotional life associated with a high metabolic rate, and often it is difficult to differentiate clearly between such a condition and mild hyperthyroidism.

For more immediate adaptation we have seen the special relationship of the suprarenal to sympathetic activity. We may then consider this gland of value in the short-lived emergency, the thyroid for more prolonged emergencies, and the pituitary for what might be called hereditary necessities for adaptation. We have seen, however, that the higher centres may affect those glands essentially designed for the requirements of exercise. It is only to be expected that similar emotions which in the lower animals precede exercise, bring about change in endocrine activity. We should expect the thyroid and the suprarenal to be most affected under these circumstances. The emotional factor is now fully appreciated in its relation to hyperthyroidism and the endocrines in general are still *sub judice* in relation to the very common condition of high blood pressure which is associated with physical and mental stress.

On the other side of the balance there is the pancreas which is concerned with the building-up, storing and preparation of energy for utilization in tissues. Since the demonstration by Banting and Best that the Islets of Langerhans in the pancreas supply an internal secretion and since the subsequent preparation of insulin, a large amount of information has been gathered regarding the rela-

tionships of these glands to the endocrine system and the results of many previous physically unconnected experiments have been amply supported. The evidence is that the gland is intimately connected with the metabolism of carbohydrates. If its secretion is absent carbohydrates are not burnt and sugar accumulates in the blood (see page 246). On the other hand, if an excess of insulin be injected, sugar disappears from the blood, apparently by being built up into another substance, no doubt in the direction of glycogen or fat. It had previously been considered that the mere increase of blood-sugar tended to produce fat and this, according to Van Noorden, accounted for the increase in weight which admittedly often precedes diabetes. Whether, however, as he suggested, excessive eating of carbohydrates prior to the disease is responsible for its onset does not appear to be certain.

The relationship of the pancreas to the endocrine organs of the other side of the balance is seen by the fact that if the latter is stimulated, either experimentally or clinically, there is evidence of pancreatic inefficiency. Actual evidence may, for convenience, be thus summarized: pituitary puncture, injection of pituitary extract, first stage of acromegaly, exophthalmic goitre, the injection of adrenaline, puncture of the floor of the fourth ventricle, splanchnic stimulation, increased carbon dioxide as in asphyxia, all cause increased blood-sugar and possibly glycosuria.

Further, thyroidectomy renders an animal more sensitive to insulin, for the latter will prevent the fatal effects of thyroid feeding, while in myxœdema there is increased sugar tolerance.

From what has been written concerning the activity side of the balance, it is reasonable to consider that by its action sugar is thrown into the blood for increased muscular work. The inhibition of the pancreas is, however, much less than in diabetes. If this work does not take place the extra sugar is not used and glycosuria may result. We know, for example, that immediately after severe physical exercise, glycosuria is not uncommon. We may consider the sympathetic activity, carbon dioxide and adrenaline to be responsible for this.

The other natural emergency with which the body has to deal is pregnancy and here again we see increased action on the activity side of the balance.

As this concerns the energy usage and storage of the individual it is dealt with further in relation to "Body Weight."

If the essential nature of the balance and its significance in relation to these two universal requirements of animals are as indicated, the interrelationships of the main endocrine organs appear easy to understand. The balance is as clear

as that between the sympathetic and parasympathetic systems. We are as yet unaware of the part played by such organs as the thymus and parathyroids, although the latter appears to be closely related to the metabolism of calcium and guanidine.

We can also begin to understand the symptoms of those diseases which affect or may affect the ductless glands. Apparently the sympathetic is closely related to the activity side and the parasympathetic to the rest side. A large number of the symptoms, for example, of thyroid disease can be thus explained. Similarly also, other lesions, e.g. tumours of the mid-brain, which paralyse the sympathetic, may be explained as affecting the activity side of the balance and bringing about a condition of adiposis dolorosa, like that seen in pituitary deficiency. Since many of the clinical disturbances of the balance lead to considerable changes in body weight, the endocrine balance is dealt with further in that connection.

THE ENDOCRINE BALANCE IN RELATION TO BODY WEIGHT

Given a constant energy intake and constant output of external work, the body weight will depend on the relative amounts of energy used for basal metabolism, i.e. the output of internal work and that available for storage of glycogen and fat. With these constants it must be admitted that basal metabolism and fat deposition must vary inversely. Fat deposition we know is largely dependent on carbohydrate utilization. Now the two glands which we know to be largely responsible for basal metabolism and carbohydrate utilization are the thyroid and the pancreas respectively. And from what has been said we are not surprised to find that these two organs antagonize each other. There is, indeed, good evidence to suggest, as we shall see below, that there is a balance between the thyroid and the pancreas and that this balance, provided the energy intake and the output of external work are constant, determines body weight.

We should expect that anything which weighs the balance on the thyroid side would cause increased basal metabolism, deficient utilization of carbohydrate, deficient deposition of fat, and thinness. Anything which weighs down the pancreatic side will bring about the opposite state of affairs. Deficiency on the thyroid side will, of course, have the same effect as an addition to the pancreatic side of the balance and *vice versa*. All recent work goes to suggest that some such change in a balance does actually take place in the body, but the interest which has centred in the pancreas in relation to carbohydrate

metabolism has caused the relation of that organ to the general endocrine system to be somewhat overlooked.

The best evidence of pancreatic deficiency or increased balance to the thyroid side is diabetes. In this latter condition we have long known that carbohydrate metabolism is inadequate and that body fat is utilized as a source of energy. It might be expected that such reduction of metabolism would cause reduction of basal metabolism. Benedict has shown, however, that this is not so, in fact it is usually increased. There is, then, not only deficient pancreatic function, but also increased thyroid action and on both accounts the patient becomes thin. It should be noted that pancreatic disease often brings about a deficiency in the external secretion of the pancreas. Fat is inadequately digested and absorbed and this increases the great tendency to emaciation.

From the point of view of body weight, and fat deposition, a similar state of affairs is seen in exophthalmic goitre. There is increased action on the part of the thyroid, as is proved by the effect of the removal of the gland surgically or by X-rays. Here we have excessive basal metabolism, the production of glycosuria from the non-utilization of carbohydrates, the result of pancreatic inhibition, and the patient becomes very thin. Restoration of the balance may be achieved by reduction of thyroid action or by supplying the internal secretion of the pancreas. The former is the more reliable and usual practice, although an appreciable improvement after insulin therapy has been reported.

In myxœdema, on the other hand, the balance is in favour of the pancreas and against the thyroid. There is marked diminution in the basal metabolism, increased sugar tolerance and deposition of fat, which indicates excessive pancreatic action.

Simple over-action of the pancreas leading to a fall in basal metabolism and increased sugar tolerance with deposition of fat, has not been described, although it may conceivably exist at the menopause (page 334). We do know that if insulin is administered in diabetes we have marked recovery to normal sugar tolerance, a disappearance of the glycosuria, and a gain in weight.

More recently the antagonism between the thyroid and pancreas has been shown by the fact that thyroidectomized rabbits are more sensitive to insulin (Burn) and also that the effect of excessive thyroid feeding is counteracted by insulin (Harrison).

Evidence of the balance being effected to either side is well seen by the relation to the pituitary. Isolated facts have long been known indicating that the pituitary was related to the thyroid, and to carbohydrate metabolism. Thyroidectomy is known to cause pituitary enlargement. Both these glands be-

come enlarged in pregnancy, both become atrophied in castration, while deficiency in either brings about abnormal sexual development. The pituitary, then, comes in on the thyroid side of the balance, but what is much more striking is its inhibiting action on the pancreatic side. In 1923 Burn showed that pituitary extract counteracts insulin. This latter experiment is of especial interest as it supports much old Italian work which indicated that animals partly deprived of the pituitary develop increased sugar tolerance, a fact contradicted by Horsley, whose animals always died after the operation, and who, therefore, claimed that the Italians had not removed the pituitary sufficiently. Needling of the pituitary has also been shown to cause glycosuria, which may be explained as due to inhibition of the pancreas. This antagonism is also seen clinically when there is excessive pituitary growth, as in acromegaly, in which, if the posterior lobe is affected, there is a loss of power to utilize sugar and glycosuria results. In hypo-pituitarism (lack of the pituitary hormone), seen in an idiopathic condition, or when the posterior lobe is pressed upon by excessive growth of the anterior lobe or by tumours, there is an increased sugar tolerance and a great storage of fat. This is best known in the infantile form, and is considered a cause of gross obesity in adults.

We are then justified in considering that the thyroid and pituitary are normally antagonistic to the pancreas, so far as carbohydrate metabolism and fat storage are concerned. How and where this takes place or whether it is direct or indirect is still to be elucidated. The gonads are related to body weight, and our knowledge of the ovaries is now reasonably clear. The work of Herring and others has shown that the pituitary is greatly enlarged in pregnancy. Marshall and Dixon have shown there is a gradually increasing secretion of the pituitary hormone, and that this is responsible for the onset of labour. The stimulating effect of pituitary extract on the uterus is well known. It must not be taken that the onset of labour is brought about wholly by this means. Other factors are concerned since the injection of pituitary extract does not bring about labour in an animal not at term. Since pituitary extract antagonizes insulin, we might anticipate clinically that the balance between pancreas and pituitary is upset in pregnancy. This is found to be the case. Glycosuria is of frequent occurrence in that condition, quite apart from lactosuria, which apparently is due to the reabsorption of lactose from the breasts. From the clinical evidence we consider that the inhibition of the mother's pancreas assists in keeping the blood-sugar at a normal or slightly higher level to allow the maximum to be available for the child. About 20 per cent. of women have glycosuria about the fifth month. This must be looked upon as a functional

diabetes, as it is not necessarily associated with pancreatic disease. Other evidence that the pancreas is inhibited is the marked fall of sugar tolerance in pregnancy. Alimentary glycosuria is much more readily produced than in the normal, indeed this is occasionally used as a test for pregnancy in the first two months, although the investigation of the blood-sugar curve would now be looked upon as a more accurate means of diagnosis.

It is noticed that some pregnant women become very thin. This, however, is not a constant feature. It may be due in part to a lowered leak point on the part of the kidney. It is normally counterbalanced by a great increase in appetite and energy intake. In this condition the suprarenal cortex is also enlarged, and we know that this part of the suprarenal is specially large in the female normally. We have good reason to believe that it has an inhibitory action on the thyroid (McCarrison). The advantage of this would be to reduce the basal metabolism of the mother, so as to leave more fuel available for the child. Actually the basal metabolism of a pregnant woman is not increased until the pregnancy is well advanced, but since the fœtus is certainly growing in the early months we may presume a reduction in the metabolism of the mother apart from the fœtus.

The above correlation explains the acidosis of pregnancy, which, according to Watson, is much more prevalent than is generally supposed. Pancreatic inhibition, by increased pituitary secretion, interferes with the mother's carbohydrate metabolism. As in diabetes, fat is incompletely oxidized with the production of ketone bodies, and a so-called acidosis (ketosis). It differs from diabetes in that there is not necessarily an increase in blood-sugar or glycosuria, since the carbohydrate not required by the mother is utilized by the child.

An actual diminution in blood-sugar is indeed possible if sugar utilization by the child is excessive. This will necessarily aggravate the acidosis whatever the state of the blood-sugar. An increased carbohydrate intake ought, as in diabetes, to relieve the acidosis, and this is found by Watson to be the case. It seems very probable that the importance of the thymus in early life may be that it regulates not only the child's metabolism, but possibly also that of the mother. Until further evidence is available this can only be a conjecture, but so far as the author is aware no work has yet been done on this point.

Women after the menopause or after ovariotomy tend to become stout. Similar results can be experimentally produced in animals. This is the exact reverse of pregnancy, and may from the evidence be put down to over-action of the pancreas. It may be noted that the administration of ovarian extract is now a recognized clinical procedure. The above facts with regard to the

ovary, pituitary, and pancreas, have long been known but have not been correlated. It is evident that some such correlation is desirable even if incomplete, and the whole picture is an excellent example of how many apparently isolated facts, some collected by clinical observers, may add to our knowledge of pure physiology.

The author wishes it to be clearly understood that the general view just given is a personal one which has received as yet no active criticism or acceptance. It is put forward tentatively in the hope that interest in the subject will be stimulated. Meantime it is a skeleton on which to hang the main facts of the case.

CHAPTER XL

PHYSIOLOGICAL PRINCIPLES IN THE TREATMENT OF CERTAIN EMERGENCIES

Illness does not as a rule immediately endanger life, and the clinician has time to consider his procedure. In some emergencies, however, life is in immediate danger and it is the duty of the clinician to be prepared for them. His action depends on his knowledge, in particular, of that which has been described earlier as the essentials of life. It must not be forgotten that on the speed of the action may depend the result, for every moment the heart is getting weaker. Essentially the heart is about to fail, and the physician has to consider immediate action to prevent this failure. It may be that the cause of failure of one of the factors on which heart-action depends is temporary, hence artificial aid may be of value in tiding over the minutes of danger. But even when death in a few hours is inevitable, the prolongation of life to its utmost may be of the greatest importance for other reasons, such as in criminal cases.

A knowledge of physiology at once indicates the procedure to be carried out, but alas, the instances in which the cause of the failure is temporary are but few. Considerations of space make it impossible to deal with more than the common emergencies which threaten immediate death.

Primary Cardiac Failure.—Such an emergency occurs when the heart fails to expel its contents. This is usually the immediate result of strain put on it, by overfilling and increased peripheral resistance in the arteries, e.g. in running to catch a train. The weaker the heart muscle, however, the more liable is the strain to be effective and in a very weak heart what would be considered normal activity may prove too much for it. Such is the case in toxæmic conditions, particularly diphtheria, in which the heart may not be able to stand the strain involved in sitting up in bed. Occasionally, as in status lymphaticus, there is sudden failure of the heart from stimulation of the inhibitory mechanism. Such a stimulus may be of a very trivial nature, such as a flip on the pomum-Adami, or the stimulation may be of a more reflex nature, such as fright, grief, joy, or the drinking of cold water when overheated, etc. More commonly this is considered to be particularly liable in the early stages of chloroform anæsthesia, and for this reason many anæsthetists administer

atropine as a routine prior to operation. The weakening of the cardiac muscle may be the result of acute poisoning, but more commonly it is progressive from chronic disease of the myocardium, or from excessive strain put upon it as the result of valvular disease. It is possible clinically to get acute dilatation of the heart as a result of rapid diminution in intra-thoracic pressure, such as may occur when large quantities of fluid are renewed from the chest. Such a condition is to be avoided rather than treated.

Whatever the cause, the chances against resuscitation, if the heart has actually stopped, are very great, especially when the failure is due to over-extension. Even in the ventricular fibrillation due to an electric current recovery is possible. Cardiac massage through the diaphragm is the sole hope and only in a few thin people can this be done. Fortunately a certain number of cases, as indicated above, occur on the operating table and the surgeon may obtain rapid access to the lower aspect of the diaphragm. The heart is gently and rhythmically compressed. The assistance given to the myocardium may be sufficient to tide over the emergency. It must be remembered in such cases that it is greatly to the disadvantage of the patient that he should be lying down, as this tends to maintain the already high venous pressure, and to throw unnecessary strain on the heart.

Failure of Aortic Pressure.—The pressure in the aorta is dependent on three variables: the peripheral resistance, the blood volume, and the heart. A fall of aortic pressure, then, is both a cause and the result of cardiac failure. Where it is a result, nothing can be done, except cardiac massage, as any attempt to raise the aortic pressure by pressure on the abdomen, also raises the venous pressure, and throws a further strain on the heart. A primary failure in peripheral resistance is never sufficient to cause immediate death, but in conditions such as spinal shock it may indirectly hasten a fatal termination.

A sudden diminution of aortic pressure from hæmorrhage is an instance where physiological knowledge is of real value. The hæmorrhage has to be stopped and the blood volume restored. The application of a tourniquet, or efficient uterine massage in post-partum hæmorrhage, has saved the life of many a patient. Probably one of the most insidious forms of blood loss is that in which the individual bleeds, as it were, into his own vessels, which become excessively dilated. This may occur in severe accidents or after surgical operations.

In man the blood loss is evident from the pallor of the skin, which is brought about in an attempt to make up for the loss. In restoring blood volume we have to consider the chemistry of the blood (this is dealt with in detail

on page 127), but in an emergency elaborate detail is impossible. The accurate adjustment of the saline content to 0.9 per cent. sodium chloride is a secondary consideration, and the heat may be judged by the sense of touch. All that is required is a warm aseptic or mildly antiseptic saline, boiled sea water or boiled salt solution (half a teaspoonful of common salt to the pint) will fulfil immediate needs. With more time available gum saline or blood transfusion must be considered, and the practising clinician is well advised to have by him a litre of sterile salt solution always available. The physiology of the administration of gum saline and blood transfusion and their dangers have been already considered.

The hæmorrhage, however, may be relative rather than actual, that is, the actual volume of the blood is not reduced but the capacity of the vascular system is enlarged. Such a condition occurs in secondary wound shock, in which there may be enormous dilatation of capillaries, in childbirth, or in sudden withdrawal of fluid from the abdomen as in ascites, after which blood may accumulate in the splanchnic area, which, it is calculated, is capable of holding a third of the total blood in the body. In the latter instances the firm application of an abdominal binder is all that is required, but in secondary wound shock steps have also to be taken to make up the blood volume.

The use of drugs in circulatory collapse must be considered. The purified alkaloids of the digitalis series are of immense value, and still better is adrenaline which even more than the others constricts blood-vessels and assists in maintaining aortic pressure. Experimentally it is found to be of great value and though its action is short-lived, it is often sufficient to bridge over a critical stage. By subcutaneous administration its action, however, is not so temporary as intravenous injection would lead one to expect. No doubt many of the disappointments in relation to this drug are due to overdose when given intravenously. The drug is primarily a sympathetic stimulant, but if the stimulus is too severe there follows a period of exhaustion; in fact, use has been made of large doses of adrenaline in the production of experimental shock. The writer feels it is a duty to warn the reader against the indiscriminate use of commercial pituitary extracts in cases of circulatory collapse. There is now full evidence that many preparations cannot be relied upon to raise aortic pressure as they often contain depressor substances; indeed, not infrequently in midwifery practice they have been found to lower it. No doubt the introduction of standards by the Medical Research Council will greatly remedy this defect.

In acute cases of cardiac failure the apprehension of the patient requires

treatment as much as his actual condition. He feels that the end is near, and under the influence of such extreme emotion the heart is made to beat with great rapidity which does not necessarily increase its output, and yet causes exhaustion. The wonderful effects of small doses of morphine usually accompanied by a cardiac stimulant or tonic administered hypodermically are now well appreciated, and in some hospitals the injection of these is a routine when acute cardiac cases are admitted. Alcohol also has a great popular reputation as a cardiac stimulant, but the physiological reason for this is not quite clear. That it gives a certain amount of courage is no doubt a factor, but as it has been shown by the writer to cause a considerable fall of venous pressure experimentally, it is not impossible that this factor is of importance. If it occurs clinically it must obviously be of great value in lessening the work of the heart as will also bleeding.

Failure of Respiration.—The supply of oxygen to the heart is dependent on the large variety of factors which are dealt with in the chapter on "Breathing." The sudden failure of respiration is commonly related only to a few of these factors, and on the immediate action of the clinician depends the life of the patient. The failure may be related to (1) the respiratory centre, (2) the respiratory passages and chest, but only those sources of failure in which real benefit can be obtained are dealt with here.

Failure of the respiratory centre, as an emergency, is commonly the result of the action of anæsthetics, or drugs such as opium, and alcohol. In these cases the centre may rapidly lose its sensitiveness, and cease to act, and result in the typical signs of carbon dioxide accumulation and oxygen want. It is necessary, then, to continue respiration by artificial means, and this may require to be kept up for hours if the heart continues to beat. If in narcotic poisoning consciousness is not quite lost the carbon dioxide muscular activity is the best respiratory stimulant.

Cases of typical asphyxia occur in strychnine poisoning, tetanus, or in epilepsy where the chest wall is thrown out of action. In some cases asphyxia may be due to actual obstruction of the respiratory passages, e.g. a foreign body or water in the larynx. In asphyxia three stages are seen: in the first stage carbon dioxide begins to accumulate. Respirations are deep and laboured, ringing in the ears is complained of, the face is blue from venous engorgement and bears an anxious expression. There results a general rise of pressure in the vascular system from the action of the carbon dioxide on the blood-vessels and the stimulation of the secretion of adrenaline. Consciousness is soon lost, as the result of diminished oxygen supply to the brain, and in this, the second stage, the

conditions are exaggerated. The sphincters relax, and there are convulsions from the action of diminished oxygen on the nerve cells. In the third stage there is general enfeeblement of respirations which become irregular and gasping. Convulsions become less, and more stretching in nature. Finally respirations cease, usually five minutes after the obstruction, but the heart continues to beat for another few minutes and during these minutes there is still time for remedial action.

In the case of foreign bodies in the glottis, if they cannot be removed, immediate tracheotomy is necessary. In the case of hanging, the body must be cut down at once, and in drowning special care must be taken that no obstructing substance has been taken into the mouth during respiratory effort.

In artificial respiration an attempt is made to get the maximum amount of air in and out of the chest. In this the prone pressure method of Schafer is most effective. The individual is placed face downwards with a coat under his chest. This procedure is of advantage in cases of drowning as it facilitates the exit of water from the respiratory passages. The operator kneels beside the patient and places his hands on the lower ribs. Then by alternately lowering and raising his body he throws his weight on the ribs and thus alternately compresses and allows to expand the lower part of the patient's chest. This procedure can be kept up by one person for hours, and there is little danger from rupture of the engorged liver which may occur in other methods.

When a man is asphyxiated by drowning, laryngeal spasm may sometimes prevent the entrance of water into the lungs and resuscitation has in these cases been known after very long periods of immersion. It is to be remembered that although the individual may fall into the water, death may not be necessarily due to asphyxia but to shock, concussion, heart failure, apoplexy, exhaustion, or injuries. It is not always possible to turn the patient into a prone position as when on an operating table, and in this case Sylvester's Method is commonly used. Here the ribs are raised by traction on the pectoral muscles by alternately raising the arms of the patient from the sides and compressing them against the chest. The method may be supplemented by pressure on the lower ribs, but the danger of affecting the engorged liver must not be forgotten.

There are also certain adjuvants of value. One of the most useful is rhythmical traction of the tongue, and in anæsthesia this may be sufficient to stimulate an indolent respiratory centre. It is to be remembered in this respect that forceps which pierce the tongue cause much less subsequent pain than those which crush. Friction of the face and ribs, and smelling salts are used to stimulate the respiratory centre, but actually carbon dioxide accumulated in

the patient's blood is the best possible stimulant. The expired air of the operator blown into mouth of the patient may also be used to stimulate.

It has been pointed by Yandell Henderson that failure of respiration during anæsthesia is not infrequently due to acapnia, i.e. a washing-out of the carbon dioxide as a result of the over-ventilation which results from sensory stimulation. There is then a possibility that the heart may fail from lack of oxygen before sufficient carbon dioxide has accumulated to bring about stimulation of the respiratory centre, the sensitivity of which is reduced by the anæsthetic. To counteract this carbon dioxide is now frequently administered with the anæsthetic. Prevention, however, is better than cure, and since experimentally such acapnia can readily be prevented by causing the animal to rebreathe its own expired air, there seems to be room for the introduction of a method by which this can readily be done on patients who are tending to over-ventilate.

Body Heat.—Loss of heat to an extent which will endanger life is not such a rare occurrence as might at first sight appear. The death of a healthy man in this way is certainly rare and only occurs when the individual has been exposed to severe cold. Even in this country, however, it is estimated that 130 people die annually from exposure. Blood heat is as dependent on heat production as on heat loss (see page 283). Should heat production then be much reduced, from mal-nutrition or exhaustion, the liability to a severe fall in blood heat may be brought about by comparatively mild degrees of exposure. This liability is still further increased if the individual is under the influence of a drug such as alcohol, which not only causes unconsciousness but also increases heat loss from dilatation of skin vessels. The effect is to create a vicious circle, for a fall in body temperature itself diminishes metabolism and still further reduces heat. Thus we see that death from exposure is most likely to occur in the very old or young or those suffering from exhausted conditions whose heat production is low. For the same reason patients under an anæsthetic, whose heat-regulating centres are thrown out of order, are particularly liable to suffer from excessive heat loss. In all such cases the principle of treatment is obvious, but it is necessary to warn against the danger of burning the bed by injudicious use of artificial heat.

In those suffering from exhaustion special care has to be taken in feeding, as, in those who have been starved, the power of digestion, like all other functions, is much reduced. The giving of partially digested and easily absorbed foods is therefore indicated while there is marked enfeeblement.

Danger of overheating is for the most part confined to hot countries. In those not acclimatized an air temperature of 100° F. in the shade may be exces-

sive, while a very warm humid atmosphere prevents the normal loss of heat from the skin. In toxæmic and febrile conditions, when the heat-regulating mechanisms are thrown out of order, and sweating fails, there is also a tendency to overheating of the body. The symptoms of excessive temperature are chiefly referable to the nervous system, and death may ensue from failure of the respiratory centre. Emergency treatment is obviously the reduction of body temperature by cold applications, e.g. by wetting and fanning the body. Such applications must be stopped when the temperature has been reduced to 100° F., since it continues to fall for a short period afterwards.

Bichat, in 1798, described what he called the Tripod of Life, the heart, lungs and brain; the violent deaths in his time indicated that these organs were the most important.

Increased physiological knowledge shows us the principles on which life is based, and when life is in danger, indicates the lines along which our efforts should be directed.

APPENDIX

A. CARBOHYDRATE, PROTEIN AND FAT METABOLISM

CARBOHYDRATE METABOLISM

Carbohydrates exist naturally in many forms. The commonest are starch (vegetable and animal), cane sugar, fruit sugar, and milk sugar. Chemically they are substances which contain carbon together with hydrogen and oxygen in the same proportion as in water. They contain sufficient oxygen to oxidize the hydrogen to water, and it is only necessary to supply oxygen for the combustion of the carbon to carbon dioxide. When carbohydrates only are being consumed, therefore, the amount of carbon dioxide given off will be the same as that of oxygen taken in. Hence in the carbohydrate combustion the respiratory quotient is unity.

Carbohydrates are classified according to the number of their carbon atoms. Thus glucose, $C_6H_{12}O_6$, is a mono-saccharide, while $C_{12}H_{22}O_{11}$, lactose or cane sugar, is a disaccharide, and $(C_6H_{10}O_5)_n$, starch, is a polysaccharide. The chemical differences of these substances need not be entered into here. It is, however, occasionally necessary to differentiate between lactose and glucose clinically, as, for example, in the investigation of the nature of the glycosuria in pregnancy. They are both reducing sugars, but may readily be differentiated by their power of reduction, the differences in their osazones or by the polarimeter.

All sugars before being absorbed normally are converted into monosaccharides and eventually probably all into glucose, which is often referred to as the current carbohydrate coin of the body. It is true that if a disaccharide is ingested in excess, some, since it is soluble, will find its way into the blood, but if so it is treated as a foreign substance and excreted in the urine.

Carbohydrate metabolism begins when starch is hydrolyzed through the catalytic action of the ptyalin of the saliva into the disaccharide maltose, and into glucose. Such digestion, as we have seen, begins in the mouth, but is continued in the stomach, although the hydrochloric acid of the latter finally inhibits it.

Uncooked starch is surrounded by an envelope (fortunately seldom com-

plete) of a cellulose nature, and unless this is broken down in cooking, the starch cannot be fully digested by the saliva. Hence the well-known indigestibility of badly cooked cereals. Again, since the starch is often treated with fat, there is a difficulty in digestion, giving rise no doubt to the reputation of roasted potatoes and badly cooked pastries in causing indigestion. In such cases not only does the fat prevent the action of the saliva on the starch, but masses of such food are liable to be formed and these no doubt set up a pyloric spasm. The noted indigestibility of new bread most likely depends on this liability, which is reduced by good mastication. The carbohydrate undigested by the ptyalin is completely disintegrated, or at least should be by the amylase of the pancreatic juice which attacks the starch, together with the maltase and lactase which attack the maltose and lactose respectively. Cane sugar is converted into lævulose and glucose by the enzyme invertase. It would appear that in adults the power of digesting lactose or sugar of milk is small. Milk, then, is mainly of value to adults in virtue of its protein and fat, although possibly bacterial action may assist later in the breakdown of the lactose. There can be little doubt, in view of the large amount of carbohydrate eaten, that a large amount of it never becomes digested at all or absorbed, but is really wasted in the fæces.

On being absorbed carbohydrates are either used as fuel or stored. The storage may be as glycogen in the liver or other tissues, especially muscle, in which form it is readily available for use, or in a more permanent and less bulky form as fat. These stores can be readily drawn upon, especially the glycogen, which can be converted through the agency of the enzyme glycogenase to glucose with extreme rapidity.

The liver appears to be specially concerned in the conversion of monosaccharides such as lævulose. This is produced normally from cane sugar by the action of the invertase of the intestinal juice. Should the liver be diseased, the power of converting lævulose is reduced. If now a quantity of lævulose (say 100 grammes) is administered, this is indicated by an abnormal rise in the blood-sugar. This test is considered to be a delicate one for the estimation of liver efficiency.

Finally, the carbohydrate is burnt to carbon dioxide and water in all active tissues, lactic acid being an intermediate product. The actual combustion of the carbohydrates need not take place during the contraction of the muscle, which may occur in the absence of oxygen, but when the muscle is resting. The great advantage of this arrangement is obvious. In conditions of severe stress it may not be possible to supply the tissues with oxygen at a rate sufficient

for its requirements. This formation of a so-called oxygen debt has already been alluded to.

FAT METABOLISM

Fats are not digested appreciably until they reach the duodenum where they come into contact with the pancreatic juice and bile, by the action of which they are broken down into fatty acids and glycerins. The bile really acts as an adjuvant to the lipase or fat-splitting enzyme of the pancreatic juice. Bile is not only a strongly alkaline fluid, but its salts have a property of reducing surface tension and so rendering possible the formation of a very fine fat emulsion. The advantage of this emulsion is that it causes an enormous surface of fat to be exposed to the action of the lipase. The fatty acids formed are themselves soluble in bile, while their salts, the products of interaction of the alkali, are, like the glycerin, soluble in water. The insoluble fat, then, is in this way converted into products which are readily soluble and absorbed. The bile salts, it will be remembered, are re-utilized as cholagogues and in the bile itself keep in solution cholesterol during its passage down the liver ducts. If for any reason, possibly as a result of the products of bacterial action, the bile can no longer keep the cholesterol in solution, it is precipitated with the formation of gall-stones.

On absorption the fat is rebuilt in the intestinal wall into a fat suitable for the animal. Fatty acids may be removed or added to give the characteristic of human fat. Under experimental conditions the fats of other animals may be stored as such, but this can only be considered to take place when the fatty acid reserves of the animal have been exhausted. The neutral fat built up passes not into the portal system like the carbohydrates and amino-acids, but into the lacteals of the intestinal villi and thence into the thoracic duct, thus entering the venous system near the termination of the superior vena cava. On the right side the right thoracic duct performs a similar function. Why the fat thus short-circuits the liver is an interesting speculation.

The fat is then utilized as fuel and burnt, forming carbon dioxide and water, or is stored in the fat depots, especially in the omentum and subcutaneous tissues. The details of the oxidation of fats cannot be entered into here, and the reader is referred to larger works. Of clinical interest, however, is the fact indicated by the formula of a fatty acid, $C_{18}H_{36}O_2$ (stearic acid), that, unlike carbohydrates, fat does not contain sufficient oxygen to oxidize all its hydrogen to water, a fact which no doubt contributes to its value as an economical method of storing energy from the point of view of space. Its calorific

value is 9.3, compared with 4.1 of carbohydrate. During the combustion of fat, therefore, oxygen is necessary for the burning not only of the carbon but also of the hydrogen. The oxygen which goes to the latter and the formation of water is excreted as such and does not appear in the examination of the expired air. Hence the oxygen absorbed is in excess of that excreted as carbon dioxide, giving a low respiratory quotient (see page 188), such as occurs in diabetes in which an excessive amount of fat is utilized. The further clinical aspects are dealt with under diabetes, in which condition the faulty combustion of fats is of the most serious consequence.

METABOLISM OF PROTEIN

Exogenous Protein Metabolism.—Proteins are nitrogen-containing substances which are essential constituents of all living tissues. Their supply is then necessary to make up for wear and tear and for the growth of new tissues, although they may, if not required for this purpose, be utilized as fuel. The proteins vary greatly in chemical constitution, but they are alike in being built up of amino-acids which are themselves soluble. As the diet of man contains proteins derived from a large variety of sources, it is necessary to have a mechanism by which these proteins can be converted into the proteins of man. This is accomplished by the breaking down of the foreign proteins in the process of digestion and the subsequent absorption and building up of the amino-acids required. Those amino-acids not required are otherwise utilized.

The digestion of protein is begun in the stomach by the action of the pepsin and hydrochloric acid. The latter is secreted by the so-called oxyntic cells of the fundus, while the former is produced by the chief or peptic cells of the glands of the body and the cells of the pyloric glands. In vitro the hydrolysis of proteins by these agents can only take place so far as the peptone stage by way of the metaprotein and proteose stages. In the stomach, however, digestion does not appear to go beyond the peptone stage. Acid digestion is brought to an end at the pylorus, where the food passes into the alkaline zone of the intestine. Digestion is then continued by the alkali and trypsin of the pancreatic juice which hydrolyze the protein more completely into polypeptides and amino-acids, in which form they are absorbed. If any escape the action of the pancreatic juice, digestion is continued by the erepsin of the succus entericus. As in all such actions we believe the enzyme, the chemical constitution of which is not known, to simply act as a catalyst, hastening a reaction which will be brought about very much more slowly by the action of the hydrogen and hydroxyl ions alone.

On absorption the amino-acids are utilized according to the requirements of the body, but, as was indicated on page 186, some amino-acids are more necessary for the organism, especially when young, than others. Such amino-acids as are required for the building up of tissue are used for this purpose and the remainder are broken down to be utilized as the source of energy and fuel. This breaking down or so-called de-amination of the amino-acids takes place in all tissues. By this process ammonia is set free while the remainder of the amino-acid becomes available as fuel like any ordinary fatty acid. The relationship of an amino-acid to a fatty acid may be readily seen by the formulæ, in which it is evident that the former is simply a fatty acid in which one or more hydrogen atoms have been replaced by an amino group NH_2, e.g. CH_3CH_2COOH, proprionic acid—a fatty acid, and $CH_3CH.NH_2.COOH$, alanine—an amino-acid.

The ammonia which is formed passes to the liver, where it joins up with the readily available product of combustion carbonic acid, to form, in the first instance, ammonium carbonate, and subsequently urea, which is excreted in the urine. Thus is explained why, in acute liver disease, ammonium salts are excreted at the expense of the urea. Ammonia is similarly used as an alkali reserve for the neutralization of acids—such as the abnormal acids produced in diabetes or chronic retention of carbon dioxide. In such conditions the ammonium salts in the urine are found to be much increased, and the urea correspondingly reduced. In over-breathing the opposite occurs. There is evidence that the ammonia utilized for the neutralization of such acids does not come so directly from the proteins as the above would indicate. It may be specially formed, possibly by the kidney, for the purposes of neutralization. It can, however, only be formed from amino bodies, and at the expense of the urea, whatever the details of its actual origin.

From a clinical point of view proteins, especially those of meat, have a somewhat evil reputation in relation to the production of high blood pressure or at least in the treatment of the condition; the exclusion of meat from the diet is of recognized value. Why this is so is by no means clear. It may be that the meat contains pressor substances and the existence of pressor amines is well established. It may be, on the other hand, that the vegetable diet commonly substituted contains valuable depressor substances such as choline. There is good evidence that even the depressor substances such as histamine (produced as decomposition products from the amino-acids, e.g. from histidine) may by dilating capillaries or rendering them abnormally permeable require a compensatory arterial constriction to maintain blood pressure. That such con-

striction may eventually become excessive or lead to arterial hypertrophy seems to be a possibility by which the arterial pressure may become persistently high.

Endogenous Protein Metabolism.—This term is applied to the utilization of the protein of the body tissues which goes on from the wear and tear of structures. This may occur to a large extent under special conditions when other energy sources are deficient, but normally there is always a certain amount of tissue breakdown. Exogenous metabolism depends on diet, while the endogenous type is dependent on the general state of the body, and is much more constant. Cathcart has emphasized that it may vary considerably, for example in severe exercise, when wear and tear is increased.

Both kinds of protein give rise to urea and sulphur compounds derived from the sulphur containing amino-acid cystine. These are excreted in the urine. In the case of cystine derived from the diet, it passes by way of the portal vein to the liver, where it is oxidized to inorganic sulphates. That liberated from tissue breakdown does not pass through the liver to any extent. It therefore escapes complete oxidation, and appears in the urine as neutral sulphur.

Another characteristic of this metabolism is creatinine. This has been shown by Folin to be excreted in very constant amounts independently of the diet. So constant indeed is its concentration in the blood and urine that its estimation in these fluids has been taken as an index of kidney efficiency, although now other tests are more convenient.

Purine Metabolism.—This variety of protein metabolism which concerns the breakdown of nucleo-proteins is of special interest in relation to gout, in which there occurs deposits of uric acid in certain areas. The nucleo-proteins are derived from the nuclei of cells and are therefore plentiful in glandular structures, such as the liver, kidney, sweetbreads and the like. The uric acid which is deposited is the end product, just as urea is of ordinary proteins. Why it should become deposited in gout instead of being excreted in the urine is a very puzzling problem. In Garrod's well-known collection of cases it was seen that the condition tended to affect the male members of certain families.

That the condition is associated with an easy life, especially if combined with a too bounteous table and well-stocked cellar, is admitted. It, however, is not confined to the rich. It is almost non-existent in Scotland, a fact which suggests that the favourite national beverages play some part in the condition. Meantime the problem remains unsolved. The metabolism of nucleo-proteins has been the happy hunting-ground of the biochemist for enzymes, and it is considered that there are no fewer than twenty-six distinct varieties concerned. This is surely striking evidence that our present conception of enzyme action

requires to be fundamentally changed, so that it will allow of the substrate (possibly) to take some part in the production of the specific enzymes. (See also page 264.)

B. HYDROGEN ION CONCENTRATION

Of recent years much attention has been paid to the "reaction" of the body fluids. With the advancement of physical chemistry, it has been shown that the older terms acidity and alkalinity were merely relative and approximate. The advent of the ionic theory set up a new order of things in this matter. In other words, the idea of acidity and alkalinity is now put on a quantitative basis. This is expressed by the word "reaction," meaning the degree of acidity or alkalinity which exists in a given solution. Most salts, acids, and alkalies are dissociable bodies, that is, they break up on solution in water into separate components known as ions. It is now known that the chemical, and therefore the physiological properties of a solution depend largely on the extent to which ions are present. For example, urine is not composed of sodium chloride, phosphate, sulphate, etc., but of sodium ions, sulphate ions, chloride ions, phosphate ions, and so on. The question of acidity or alkalinity is, in principle, a matter of the degree of abundance or scarcity, as the case may be, of hydrogen ions. It is the presence of these which gives the various reactions and characteristics of these solutions. Hydrochloric acid, for example, dissociates into chlorine ions and hydrogen ions, while sodium hydroxide breaks up into sodium ions and hydroxyl ions. The extent of the dissociation is dependent on several factors, the nature of the solvent, the temperature, and the strength of the solution. Some of the solute always remains undissociated, and the amount dissociated can be expressed as a percentage for a given temperature and strength of solution. Strictly the matter is a statistical rather than a fixed one. That is, if we say a solution of hydrochloric acid is 97 per cent. dissociated, it means that at any given moment there are 3 per cent. of molecules which are in (temporary) union. A few minutes later there is still 3 per cent. united, but they would not be the same 3 per cent. as before. In other words, there are always being made temporary unions and divorces. The state of affairs is a kinetic one, and so can only be expressed in a statistical way. Even water dissociates into H and OH ions, but only to a small extent. Of course, the numbers of each of these ions are equal. It should also be mentioned that the ions are electrically charged, the charges on each ion being equal and opposite.

When the number of H and OH ions in a solution is equal, the solution is said to be neutral. If to this neutral solution a little acid is added, the number

of H ions is therefore increased over the OH ions and the solution is "acid." Conversely, if a little caustic soda is added, there is an excess of OH ions, and the solution is "alkaline." It should be noted that even in an alkaline solution there are present H ions, though they are numerically less than the OH ions. The presence of the latter is of course due to the dissociation of the water that is necessarily present.

It has been found possible to determine the number of hydrogen ions per unit volume in pure water. It amounts to 0.0000001 of a gramme per litre. This is known as the cH or the concentration of the hydrogen ions. Alkaline solutions have fewer hydrogen ions, and acid solutions more, than in the case of pure water. It is now customary and at the same time very convenient to express the actual hydrogen ion concentration (cH) as a power of ten. A further simplification consists in using only the numerical value of that power (regardless of sign). This index, devoid of sign, is designated its pH (Sorensen). Neutrality is therefore expressed as pH 7.0, while acid solutions have a pH ranging from 0 to 7.0; and alkaline solutions vary from pH to 7.0 to 14.0. It must, however, be noted that the pH scale is a logarithmic one, so that pH really stands for—log [H], that is, it represents a negative logarithm. Hence as pH increases, the acidity decreases, and *vice versa.*

A normal solution of any acid contains one gramme of hydrogen per litre. Hence a decinormal solution of hydrochloric acid would contain 0.1 gramme of hydrogen ions per litre. This, however, is only true provided the whole of the acid has dissociated, which is not usually true. It can be shown that in this case the acid molecules are 91 per cent. dissociated, and the cH is thus not 10^{-1}, but 91 per cent. of 10^{-1}, that is, 0.091. Converted into pH, that is to —log [H], it becomes 1.04 (instead of 1.0). A weak acid or a weak base is one which ionized but little; good examples are those of lactic, or acetic acid. A salt derived from any such weak acid or base is more highly ionized than that from which it has been formed. This is of importance in that if the free ion has a different colour from the un-ionized acid or base there will be a colour change on converting the acid or base into a salt. We shall revert to this again below.

Since the ionization is a matter of electrical charges and their attractions, it is clear that the fundamental way of determining the hydrogen ion concentration of a solution would be an electrical one. This in fact is the case, the reaction being determined from the electro-motive force set up between a hydrogen electrode and the free ions in solution. The electrode is really a piece of platinized wire surrounded by an atmosphere of hydrogen and just

dipping into the solution whose reaction has to be found. This is an elaborate and highly technical way of finding the pH and in practice one requires a more rapid and explicit means of so doing. By using the principle mentioned above, namely, that a free ion may have a different colour from the un-ionized acid or base from which it is formed, a very much more convenient way of determining the hydrogen ion concentration of a solution may be devised. This colorimetric method is dependent on the use of such salts as just stated and known as "indicators." Large numbers of them are now in use, each having its own "range of action." For example, phenolphthalein is colourless in acid solution, the degree of acidity being not less than pH 8.0 or thereabouts, while if in alkaline solution it becomes pink. Therefore 8.0 is a transition point, and the mere addition of a little of this indicator to a solution will immediately tell whether or not its reaction is of a pH greater or less than 8.0. Of course, to go into more detail one must have a set of such indicators, whereby it will be possible to gradually narrow down the range of action until we can state quite definitely the pH within quite narrow limits.

Some of the more usual indicators are phenol red (6.8 to 8.4), yellow to red; methyl orange (3.1 to 4.4), red to yellow; Congo red (3.0 to 5.0), red to blue; thymol phthalein (9.3 to 10.5), colourless to blue, and thymol blue in its acid range (1.2 to 2.8), changing from red to yellow, while on its alkaline range (8.0 to 9.6) it changes from yellow to blue. A few drops of any of these indicators may then be added to a fluid of unknown reaction and the colour compared with a standard series of solutions of known and graded hydrogen ion concentration. By this means it is possible to quickly determine the pH of a solution. To give some idea of the nature of the results obtained, the following is a list of the usual pH values of some common biological fluids: Gastric juice, 1.77; urine, 5.5 to 7.0; human milk, 7.0: saliva, 6.9; blood plasma, 7.4; pancreatic juice, 8.3.

We may add that a certain amount of technical skill is required if the pH is to be accurately found. This is more particularly the case with the determination of the reaction of blood. For details the reader must consult special textbooks.

C. THE RESPIRATORY FUNCTION OF THE BLOOD

On the Carriage of Oxygen.—The carriage of oxygen from the lungs to the tissues and the removal of carbon dioxide in the opposite direction are essential to life. Thus, for its vital functions, the body depends to a large extent on the blood, which not only has a respiratory function but also carries

nourishment and water to the tissues. So long as there is actual fluid in the blood-vessels this latter function may be carried out. When we deal, however, with the carriage of oxygen and carbon dioxide we find that the mechanism responsible not infrequently becomes deranged. Although the carriage of oxygen is largely affected by the presence of carbon dioxide and *vice versa*, it is well in the first instance to consider them separately.

While it is true that any watery fluid is able to carry a certain amount of oxygen in simple solution, it would be quite impossible for the large amounts of oxygen required by the body to be carried in this way. It can be experimentally demonstrated that if the blood of a frog is replaced by saline solution, and the animal kept in an atmosphere of oxygen, it may continue to live reasonably normally. As, however, the atmosphere only contains 21 per cent. of oxygen it would be impossible for the animal to live except in a special chamber. For the purpose of carrying gas, therefore, a special chemical substance, hæmoglobin, has been utilized. As a result the blood is capable of carrying forty times the amount of oxygen it would otherwise do. The hæmoglobin enters into chemical combination with the oxygen, and carries it to the tissues. Here the action is reversed, i.e. dissociation occurs and the oxygen is set free. The reaction may be represented thus:

$$Hb + O_2 \rightleftarrows HbO_2$$

or, in words, hæmoglobin plus oxygen produces oxyhæmoglobin.

It can be demonstrated that if blood is exposed to air containing 21 per cent. of oxygen and allowed to take up its full complement, the latter amounts to 18.5 c.c. per 100 c.c. of blood. This may be done either by exposing the blood to a vacuum or by the addition of potassium ferricyanide. Alveolar air, be it noted, has an oxygen content of 13 per cent., the outside air being as stated, 21 per cent. This is due to the fact that blood is constantly taking up oxygen from the alveoli, and at each respiration only a part of the alveolar air is replaced. If blood is exposed to a mixture of oxygen and nitrogen at atmospheric pressure containing this concentration of oxygen, it is found that it still takes up 17.3 c.c. Should the mixture contain carbon dioxide (which tends to reduce the amount held) to an extent approximating that which normally exists in the alveoli, it is found that as much as 13.5 c.c. are taken up until the oxygen falls to 9 per cent. Thus we see that the capacity for hæmoglobin to take up oxygen is not only very great, but in atmospheres containing very wide percentages of oxygen it will take up over 90 per cent. of the amount of which it is capable. The importance of this is seen in relation to oxygen therapy, and obviously it may be of enormous advantage to the animal.

Now when we consider the giving up of O_2 we have to consider the percentage of oxygen in the tissue fluids and from the point of view of taking up or giving up this gas it matters not whether it is in a mixture with other cases or dissolved in fluids. In the tissues the percentage of oxygen is less than 5 per cent., and commonly less than 1 per cent., depending on the activity of the tissues and their oxygen requirement. At these percentages, however, the power of the hæmoglobin to hold oxygen is very small. Indeed, if 100 c.c. of blood are exposed to a mixture containing 1 per cent. oxygen and carbon dioxide even to the extent to which it is in arterial blood, it will take up only about 2 c.c. Thus in the body, if the blood has been loaded to the extent of 17.3 c.c. per 100, when it arrives at the tissues the additional oxygen is given off, if need be. In severe exercise the oxygen in the tissues may fall to zero and then the whole of the 17.3 c.c. carried by each 100 c.c. of blood may be set free, but at rest, as the tissue fluids contain about 5 per cent. of oxygen, the blood in the veins holds still some 13 c.c. and only 4 c.c. of oxygen are yielded.

These percentages may be expressed graphically in the dissociation curve of blood. Here the rapid falling-off in the amount of oxygen taken up by hæmoglobin, if exposed to percentages under 7 per cent., is clearly seen and the almost negligible quantities which are held are percentages under 1 per cent., which gives the curve a characteristic "ʃ" shape.

This taking in and giving up of oxygen is further facilitated by other factors. Acids such as lactic acid and carbon dioxide noticeably reduce the amount of oxygen held by the blood, although they do not interfere to any extent with the amount taken in at the higher percentages. Similarly, salts and temperature make a marked difference, not only in the rate at which the exchange takes place, but they also increase the dissociation of the oxyhæmoglobin. It is to be noted that in exercise both heat and carbon dioxide are produced in the tissues which thereby directly facilitate their own oxygen supply when this is desired, quite apart from that brought about by the action of the carbolic acid on the respiratory and circulatory systems.

What has been said above refers to normal life at pressures approximately that of sea-level (760 mm., barometric pressure). If we consider life at high altitudes the matter is a little more difficult. Although possibly this condition does not come into the purview of many physicians, it has of recent years been a matter of general interest. As we ascend, the barometric pressure decreases 25 mm. approximately for each 900 feet. At 10,000 feet, then, the barometric pressure, instead of being 760 mm., is approximately 490 mm. The relative percentages of the constitution of the gases in the air remains the same, but a

similar amount of oxygen occupies a very much larger space. To use an analogy, suppose we stir up a mixed dust of red and blue particles, the relative percentages of each variety of particle may remain the same, but we would be able to collect much less of the dust in a given space at a distance from its source than nearer. Thus we see how 13 per cent. of oxygen at 10,000 feet, so far as the amount of oxygen is concerned in a given volume, is but equal to 7 per cent. at sea-level. It is customary to express these percentages in terms of partial pressure. Thus at an atmospheric pressure of 760 mm. the 13 per cent. of oxygen which occurs in the alveoli will have a partial pressure of 100, but at 10,000 feet, where the barometric pressure is but 490 mm., the partial pressure is but 53.7. As it is found that the same physical laws which govern the solution of gases in a liquid apply to the taking up of oxygen by hæmoglobin, the amount of oxygen which will be taken in will depend not only on its solubility in blood but on its partial pressure. At half the pressure only half the amount will be taken in. Thus we see that at 10,000 feet, where there is much less oxygen, the blood will take up very much less oxygen than it does at sea-level. We need but refer to the dissociation curve to see what a difference the partial pressure would make on the amount of oxygen taken up.

The body attempts to compensate for this deficient supply of oxygen by accelerating the circulation and this it does with considerable success. It cannot, however (although the normal amount of oxygen is transported per minute), make up for the fact that the oxygen is loaded at an insufficient tension to which the respiratory centre is specially sensitive. This has been already considered. We have also seen that the amount of carbon dioxide appreciably affects the amount of oxygen which the blood can take up, while the amount of carbon dioxide carried by the blood is likewise affected by its oxygen content.

The Carriage of Carbon Dioxide by the Blood.—Just as the blood is specially adapted for the carriage of oxygen, so also is it adapted for the carriage of carbonic acid, for, just as in the case of oxygen, the body requires so much to be transported that it would be impossible to depend purely on the solution of the gas in the blood. Further, the blood would become acid in reaction and this would be incompatible with life. The actual method by which carbonic acid is carried has been a matter of considerable controversy in the past, but most authorities agree that for the most part carbon dioxide from the tissues to the lungs is carried in combination with sodium as sodium bicarbonate ($NaHCO_3$) and a small amount in solution. The sodium bicarbonate is faintly alkaline and the carbonic acid, H_2CO_3 (i.e. Water + CO_2) is, of course, acid. A balance, therefore, is effected, so that there is no disturbance

of the neutrality of the blood provided the amount of carbon dioxide in solution is not in excess. The hydrogen ion concentration of the blood, therefore, may be considered to depend on the ratio $\frac{H_2CO_3}{NaHCO_3}$. Here there must be a reserve of sodium in the blood for the purpose of uniting with the carbon dioxide and this alkali we understand as the "alkali reserve" of the blood. Now hæmoglobin itself is an acid, but oxyhæmoglobin is a stronger acid, and as such these substances compete with the carbonic acid for the available alkali. We have seen, however, that the oxyhæmoglobin formed in the lungs is reduced in the tissues to hæmoglobin, and as these substances are not of an equal acidity, it is evident that the competition with the carbonic acid is not a constant one. It is therefore possible for a certain amount of the alkali to alternate, as it were, between the oxyhæmoglobin and the carbon dioxide. In the tissues then, where the oxyhæmoglobin is diminished, the carbon dioxide is able to combine with the sodium to form sodium bicarbonate, while in the lungs the oxyhæmoglobin becomes attached to the alkali and carbon dioxide is given off. Or, it may be said that carbon dioxide is given off, and the oxyhæmoglobin becomes attached to the then available alkali. We have already seen that the less carbonic acid there is in the blood the more oxygen it can contain, and conversely.

The alkaline phosphates can also be made use of to provide sodium, as is seen in relation to the "Neutrality of the Blood," while the proteins of the plasma also supply a small amount of alkali.

We have now given a somewhat general idea of how this carbon dioxide is carried, but unfortunately the actual mechanism is not quite so simple. The alkali in the plasma is largely sodium, but the alkali in the corpuscles is largely potassium and the alkalies do not pass through the walls of the corpuscles readily. The adjustment, therefore, between the corpuscles and plasma has to be made by the transference of more readily diffusable ions, especially chlorine. In the first instance we may look upon the carbon dioxide (in solution) as acting upon the sodium chloride of the plasma to form bicarbonate and hydrochloric acid thus:

$$NaCl + CO_2 + H_2O = NaHCO_3 + HCl.$$

The hydrochloric acid formed passes at once into the corpuscles to react with the available alkali—in this instance potassium—set free in the reduction of oxyhæmoglobin to hæmoglobin, the latter being a weaker acid. The reactions may be indicated thus since we do not as yet know the formula of hæmoglobin—

$$K_2HbO_2 + HCl = KCl + Hb + O_2$$

and $$K_2HPO_4 + HCl = KCl + KH_2PO_4.$$

The increased acidity of the acid phosphate is here counterbalanced by the decreased acidity of the hæmoglobin.

From these facts it is evident that the plasma of venous blood contains less chlorides than that of arterial blood, while the corpuscle contains more. Also the sodium which carries the dioxide to the lungs passes back to the tissues as sodium chloride. A small amount of carbon dioxide itself may enter the corpuscle and, acting like the hydrochloric acid, may bring about a similar reaction. It is evident that the carbon dioxide facilitates the liberation of the oxygen. This we know to be the case from what has been stated in relation to oxygen transport. When the blood reaches the lungs it is exposed to conditions where the percentage of carbon dioxide is appreciably lower and that of oxygen higher than in the tissues. These gases are therefore exchanged and to permit of all this the processes described above are reversed.

SELECTED BIBLIOGRAPHY

In this list are given *only* those most recent books in which references to original papers are to be found, and which are easily available.

General

Bayliss, *Principles of General Physiology,* edited by A. V. Hill. Longmans, 1925, pp. 881.

A standard work in which the physical and chemical processes concerned in animal and plant life are described in their more scientific aspects.

Beaumont and Dodds, *Recent Advances in Medicine.* Churchill, 1925, pp. 302.

Gives excellent workable descriptions of the more modern methods of diagnosis and treatment, with remarks concerning their usefulness. The best small advanced laboratory manual for general purposes.

Cushny, *A Textbook of Pharmacology and Therapeutics.*

A standard work in this subject.

Evans, Lovatt, *Recent Advances in Physiology.* Churchill, 1925, pp. 360.

The recent advances in the physiology of the blood corpuscles, the carriage of carbon dioxide, and the reactions of the blood, the output of the heart, muscle contraction, the active principles of some endocrine organs, the labyrinth, conditioned and postural reflexes are dealt with from the scientific aspect.

Hawk, *Practical Physiological Chemistry.* Churchill, 1923.

Luciani, *Human Physiology,* translated by Welby, 5 vols. Macmillan.

Contains a valuable record, especially of early Continental work until 1909.

Macleod, *Physiology and Biochemistry in Modern Medicine.* Kimpton, 1925, pp. 971.

An advanced textbook dealing with the physico-chemical basis of physiological processes, circulation, respiration, blood and lymph, circulation of blood, digestion and metabolism, urine, endocrine organs, nervous system, especially from the point of view of the laboratory.

Parsons, *Fundamentals of Biochemistry in relation to Human Physiology.* Heffer, 1924, pp. 212.

A short introduction to Biochemistry in which the principles of the subject are put forward with singular clearness and attractiveness.

Roaf, *Physiological Chemistry.* Methuen, 1921, pp. 212.

This book gives a brief readable account, from the more scientific aspect, of the chemical processes which take place in living organisms.

Schafer (ed.), *A Textbook of Physiology,* by British Physiologists, 2 vols. Oxford University Press, 1900.

Contains the most complete statement of work and references till 1900.

Short, Rendell, *The New Physiology in Surgical and General Practice.* Wright, 1922, pp. 313.

A very readable but brief account of those parts of the subject of more surgical interest.

The Nervous System

Behan, *Pain—its Origin, Conduction, Perception and Diagnostic Significance.* Appleton & Co., 1920.

Brown, Langdon, *The Sympathetic Nervous System in Disease.* Oxford Medical Publications, 1923.

Cannon, *Bodily Changes in Pain, Hunger, Fear and Rage.* Appleton, 1925.

Cobb, "Review on the Tonus of Skeletal Muscle," *Physiol. Revs.*, 1925, 5.

Feiling, "Symptoms of Nervous Disease," Goulstonian Lectures, *Lancet*, 1922, 775.

Gaskell, *The Autonomic Nervous System*, Monographs of Physiology. Longmans, 1920.

Head, "Certain Aspects of Pain," *B.M.J.*, 1922, I.

Herring, "Regulating and Reflex Processes," *B.M.J.*, 1923.

Horrax, "Contributions of the War to the Physiology of the Nervous System," *Physiol. Revs.*, 1921, 1.

Langley, *The Autonomic Nervous System*, Part 1. Heffer, 1921.

Lucas, *The Conduction of the Nervous Impulse*, Monograph on Physiology. Longmans, 1917.

Mackenzie, *Symptoms and their Interpretation.* Shaw, 1921.

Magnus, "Animal Posture," Croonian Lecture, *Proc. Roy. Soc.*, B. 1925, 98, 339.

Medical Research Council Report, No. 54, "The Diagnosis and Treatment of Peripheral Nerve Injuries."

Pike, "The Functions of the Vestibular Apparatus," *Physiol. Revs.*, 1923, 3, 209.

Pottenger, *Symptoms of Visceral Disease.* Kimpton, 1925.

Ransom, "Afferent Paths for Visceral Reflexes," *Physiol. Revs.*, 1921, 1.

Riddoch, *Reflex Functions of the Spinal Cord.* Brain, 1917, 40, 264.

Sherrington, *The Integrative Action of the Nervous System.* Constable, 1921.

Sollman, "The Pharmacology of the Autonomic Nervous System," *Physiol. Revs.*, 1923, 2.

Tinel, *Nerve Wounds Symptomatology of Peripheral Nerve Lesions.* Ballière, Tindall & Cox, 1918.

Trotter, "Pain," *Med. Sc. Abs. & Reviews*, 1921, 4, 43.

Walsh, Riddoch and Others, "Physiology of Symptom Production," *B.M.J.*, 1921, 837.

Wilkinson and Gray, *Mechanism of the Cochlea.* Macmillan, 1924.

Wilson, S. A. K., *Aphasia*, Psyche Miniatures, Medical Series. Kegan Paul, 1926.

Circulation

Bainbridge, *Physiology of Muscular Exercise*, edited by Anrep, Monographs of Physiology. Longmans, 1925.

Bayliss, *The Vasomotor System*, Monographs of Physiology. Longmans, 1923.

Bolton, "Pathology of Dropsy," *Jour. Path. and Bact.*, 1903, 1909, 1916.

Cowan and Ritchie, *Diseases of the Heart.* Edward Arnold & Co., 1922.

Dale, "The Activity of the Capillaries in relation to certain forms of Toxæmia," Oliver-Sharpey Lectures, *B.M.J.*, 1923, 1.

Eyster and Meek, "The Origin and Conduction of the Heart Beat," *Physiol. Revs.*, 1921, 1.

Flint, *The Heart—Old Views and New.* Lewis, 1921.

Garrey, "Auricular Fibrillation," *Physiol. Revs.*, 1924, 4.
Henderson, Yandell, "Volume Changes of the Heart," *Physiol. Revs.*, 1923, 3.
Hill, L., *Physiology and Pathology of the Cerebral Circulation.* Churchill, 1896.
Hooker, "Evidence of Functional Activity on the part of the Capillaries and Vesicles," *Physiol. Revs.*, 1921, 1, 112.
Krogh, *Anatomy and Physiology of the Capillaries.* Yale Univ. Press, 1923.
Lewis, *Clinical Electrocardiography.*. Shaw, 1925.
——— *Clinical Disorders of the Heartbeat.* Shaw, 1926.
——— *Mechanism and Graphic Registration of the Heartbeat.* Shaw, 1925.
MacCallum, "Arterial Sclerosis," *Physiol. Revs.*, 1922, 70.
Mackenzie and Ott, *Principles in the Diagnosis and Treatment of Heart Affections.* Oxford University Press, 1923.
McWilliam, "Blood Pressure in Man under Normal and Pathological Conditions," *Physiol. Revs.*, 1925, 303.
Medical Research Council Reports, No. 25, "Woundshock and Hæmorrhage"; No. 26, "Traumatic Toxæmia as a Factor in Shock"; No. 27, "Blood Volume Changes in Wound Shock and Primary Hæmorrhage."
Starling, *The Law of the Heart,* Linacre Lecture. Longmans, 1918.
Wiggers, "The Regulation of the Pulmonary Circulation," *Physiol. Revs.*, 1921, 319.
——— *The Circulation in Health and Disease.* Lea & Febiger, 1923.
Here the matter is dealt with from the more experimental standpoint and there is appended to each chapter what is probably the most complete bibliography of this subject in existence.

Respiration and Muscular Exercise

Bainbridge, *Physiology of Muscular Exercise,* edited by Anrep. Longmans, 1925.
Barcroft, *The Respiratory Function of the Blood.* Cambridge University Press, 1914.
——— "Anoxæmia," British Association Address, 1920.
Coke, *Asthma.* Wright, 1923.
Fletcher and Hopkins, "The Respiratory Process in Muscle and the Nature of Muscular Movement," Croonian Lecture, *Proc. Roy. Soc.*, 1917. B. 89, 44.
Gesell, "The Chemical Regulation of Respiration," *Physiol. Revs.*, 1925, 5.
Haldane, *Respiration,* Yale University Press, 1922.
Krogh, *The Respiratory Exchange in Animals and Man,* Monographs on Biochemistry. Longmans.
Lundsgaard and Van Slyke, *Cyanosis,* Medicine Monographs. Williams & Wilkins, 1924.
Hill, "The Mechanism of Muscular Contraction," *Physiol. Revs.*, 1922, 2, 343.
Meakins, Various Papers, *B.M.J.*, 1920-24.
——— and Davies, *Respiratory Function in Disease.* Oliver & Boyd, 1925.
Means, *Dyspnœa,* Medicine Monographs. Williams & Wilkins, 1924.
Medical Research Council Report, No. 72, "The Acid-Base Equilibrium of the Blood."
Van Slyke, "The Carbon Dioxide Carriers of the Blood," *Physiol. Revs.*, 1921, 1, 141.

The Neutrality of the Body

Clark, *Determination of Hydrogen Ions.* Williams and Wilkins, 1923.

Henderson, Yandell, "The Physiological Regulation of the Acid Base Equilibrium of the Blood and some related functions," *Physiol. Revs.,* 1925, 5.

Medical Research Council, Report 72, "The Acid Base Equilibrium of the Blood," 1923.

Shohl, "Mineral Metabolism in Relation to Acid Base Equilibrium," *Physiol. Revs.* 509.

Van Slyke, "The Carbon Dioxide Carriers of the Blood." *Physiol. Revs.,* 1921, 1

Wright, "Neutrality Regulations in the Body," *Physiol. Revs.,* 1923, 3.

The Urinary System

Cushny, *The Secretion of Urine,* Monographs of Physiology. Longmans, 1926.

Head and Riddoch, *On the Control of the Bladder.* Brain, 1917, 40.

Kidd, *Common Infections of the Kidneys.* Oxford University Press, 1920.

Maclean, *Modern Methods in the Diagnosis and Treatment of Renal Disease.* Constable, 1924.

McNider, "A Review of Acute Experimental Nephritis," *Physiol. Revs.,* 1924, 4.

The Digestive System

Bayliss, *Nature of Enzyme Action,* Monograph on Biochemistry. Longmans, 1919.

Beatty, *The Method of Enzyme Action.* Churchill, 1917.

Bennett, *The Stomach and Upper Alimentary Tract in Health and Disease.* Heinemann, 1925, pp. 343.

Bolton, Duodenal regurgitation, *Lancet,* 1922, 1, 420, and *B.M.J.,* 1923, 2.

Carlson, *The Control of Gastric Juice in Health and Disease.* Univ. of Chicago Press, 1917.

——— "The Control of Hunger in Health and Disease," *Physiol. Revs.,* 1923, 3.

Goldsmidt, "Absorption from the Intestine," *Physiol. Revs.,* 1921, 1, 421.

Hurst, "The Sphincters of the Alimentary Canal," *B.M.J.,* 1925, 145.

——— *The Sensibility of the Alimentary Canal in Health and Disease,* 1917.

——— *Digestion and Nervous Diseases, Addison's Disease and Asthma.* Heinemann, 1924.

Lawrence, *The Diabetic Life.* Churchill, 1925.

This is the most complete small monograph on the control of diabetes by diet and insulin.

Leyton, *Diabetes Mellitus (The Allen Treatment).* Adlard, 1923.

Marshall, "The Etiology of Dental Caries," *Physiol. Revs.,* 1924, 4.

Moynihan, *Two Lectures on Gastric and Duodenal Ulcers.* Wright, 1923.

Pavlov, *The Work of the Digestive Glands,* translated by Thomson. Griffin, 1910.

Starling, *Recent Advances in the Physiology of Digestion.* Constable, 1911.

Stewart, "Pathology of Gastric Ulcer," *B.M.J.,* 1923, 955.

Diet and Metabolism

Barger, *The Simple Natural Bases,* Monographs on Biochemistry. Longmans, 1921.

Benedict and Co-workers, Publications of the Nutritional Laboratory of the Carnegie Institute of Washington.

Boothby and Sandiford, "Basal Metabolism," *Physiol. Revs.,* 1924, 4, 69.

Bloor, "Fat Transport in the Body," *Physiol. Revs.*, 1922, 2.
Cathcart, *The Physiology of Protein Metabolism,* Monographs on Biochemistry. Longmans, 1921.
——— "The Influence of Work on Protein Metabolism," *Physiol. Revs.*, 1925, 5.
Chalmers-Watson, *Food and Feeding in Health and Disease.* McDougall, 1915.
Dakin, *Oxidations and Reductions in the Animal Body,* Monographs on Biochemistry. Longmans, 1924.
Drummond, Lectures on Oxidations, Phosphates and Vitamins, *Certain Aspects of Biochemistry,* Univ. of London Press, 1926.
Garrod, *Inborn Errors of Metabolism.* Oxford University Press, 1923.
Harding, "Metabolism in Pregnancy," *Physiol. Revs.*, 1925, 5.
Hill, Leonard, *Sunshine and Open Air.* Arnold, 1926.
Hindhead, *Proteins and Nutrition.* Seymour & Co.
Hunter, "Creatine and Creatinine," *Physiol. Revs.*, 1922, 2, 586.
Hutcheson, R., *Food and the Principles of Dietetics.* Arnold, 1922.
Leathes and Raper, *The Fats,* Monographs on Biochemistry. Longmans, 1925.
Lewis, "Sulphur Metabolism," *Physiol. Revs.*, 1924, 4.
Lusk, Graham, *Elements of the Science of Nutrition.* Saunders, 1921.
——— and Co-workers. Publications from the Russell-Sage Institute of Pathology, New York.
Macleod, "The Sugar of the Blood," *Physiol. Revs.*, 1921, 1, 208. See also Carbohydrate Metabolism and Insulin.
McCann, *Calorimetry in Medicine,* Medicine Monograph. Williams & Wilkins, 1924.
McCarrison, *Studies in Deficiency Disease.* Oxford University Press, 1921, and Various Papers in the *B.M.J.*, especially from 1922.
Medical Research Council Reports, No. 38, "The Present State of our Knowledge Concerning Excessive Food Factors (Vitamins)," 1919.
Medical Research Council Reports on Rickets. No. 20, by Findlay and Ferguson; No. 61, by Mellanby; No. 68, by Mann, and No. 71, by Korenchevsky.
Plimmer and Plimmer, *The Vitamins and Choice of Food.* People's League of Health, 1924.
Rose, "Purine Metabolism," *Physiol. Revs.*, 1923, 3, 544.
Talbot, "Basal Metabolism of Children," *Physiol. Revs.*, 1925, 5.

Liver, Bile, Etc.

Brown, Langdon, "The Value of Laboratory Tests in Diseases of the Liver and Pancreas," *B.M.J.*, 1923, 461.
Mann, "The Functions of the Gall Bladder," *Physiol. Revs.*, 1924, 4.
Maximow, *Physiol. Revs.*, 1924, 4, 533.
McNee, *Quart. Journ. Med.*, 1923, 390.
——— Van den Bergh, Wilcox and Others, "Discussion on Jaundice," *B.M.J.*, 1924, 499.
Rich, "The Formation of Bile," *Physiol. Revs.*, 1925, 5.
Rolleston, "Degenerative Diseases of the Liver," *B.M.J.*, 1922, 1055.
Rous, "The Destruction of Red Blood Corpuscles in Health and Disease," *Physiol. Revs.*, 1923, 3, 75.
Whipple, "The Origin and Significance of the Constituents of the Bile," *Physiol. Revs.*, 1922, 2.

The Internal Secretions

Campbell and Macleod, *Insulin*, Medicine Monographs. Williams & Wilkins, 1924.
Dale, The Chemical Control of Certain Bodily Functions, *Certain Aspects of Biochemistry*. Univ. of London Press, 1926.
Hoskins, "The Relation of the Adrenals to the Circulation," *Physiol. Revs.*, 1922, 2, 343.
Kellaway and Cowell, *Journ. Physiol.*, 1922, 57, 82.
McCarrison, *Studies in Deficiency Disease*. Oxford University Press, 1921, and Various Papers in the *B.M.J.*
——— *The Thyroid Gland in Health and Disease*. Ballière, Tindall & Cox.
Macleod, *Carbohydrate Metabolism and Insulin*, Monographs on Physiology. Longmans, 1926.
Marine, "The Present State of the Function of the Thyroid," *Physiol. Revs.*, 1922, 2, 521.
Marshall, "The Internal Secretions of the Reproductive Organs," *Physiol. Revs.*, 1923, 3.
Sharpey-Schafer, *The Endocrine Organs*, Pts. 1 and 2. Longmans, 1925-6.
Vincent, Swale, *The Internal Secretion and the Ductless Glands*. Edward Arnold & Co., 1924.
——— "Critical Examination of the Current Views on the Internal Secretions," *Lancet*, 1922, 313.
Vines, H. W. C., *The Parathyroid Glands in Relation to Disease*. Arnold, 1924.

The Temperature of the Body

Barbour, "The Heat-Regulating Mechanism of the Body," *Physiol. Revs.*, 1921, 1, 295.

The Blood

Barcroft, *The Respiratory Function of the Blood*. Cambridge Univ. Press, 1914.
——— "The Significance of Hæmoglobin," *Physiol. Revs.*, 1924, 4.
Buckmaster, *The Morphology of Normal and Pathological Blood*. Murray, 1906.
Bond, *The Leucocyte in Health and Disease*. Murray, 1906.
Bunting, "The Leucocytes," *Physiol. Revs.*, 1922, 2.
Folin, "Non-Protein Nitrogen of the Blood in Health and Disease," *Physiol. Revs.*, 1922, 2.
Gulland and Goodall, *The Blood, a Guide to its Examination and to the Diagnosis and Treatment of its Diseases*. Green, 1926.
Macleod, "The Sugar of the Blood," *Physiol. Revs.*, 1921, 1.
Maximow, "Relation of Blood Cells to Connective Tissue and Endothelium," *Physiol. Revs.*, 1924, 4, 533.
Myers, "Chemical Changes in the Blood and their Clinical Significance," *Physiol. Revs.*, 1924, 4.
Ponder, *The Erythrocyte and the Action of Simple Hæmolysins*, Biological Monograph. Oliver & Boyd, 1922.
Sabin, "On the Origin of the Cells of the Blood," *Physiol. Revs.*, 1922, 2.
de Wesselow, *The Chemistry of the Blood in Clinical Medicine*. Benn, 1924.

Blood Groups

Beaumont and Dodds, *Recent Advances in Medicine.* Churchill, 1925.
Dykes, Blood Groups, *Lancet,* 1922. 271 and 579.

Blood Volume and Œdema

Erlanger, "Blood Volume and its Regulation," *Physiol. Revs.,* 1925, 1.
Loeb, *Œdema,* Medicine Monographs. Williams and Wilkins, 1925.
Marriott, "Anhydremia," *Physiol. Revs.,* 1923, 3.
McLean, "Œdema as a Problem of Physiological Regulation," *Physiol. Revs.,* 1925, 5, 618.
Rowntree, "The Water Balance of the Body," *Physiol. Revs.,* 1922, 2.
Starling, *The Fluids of the Body.* Constable, 1909.

Blood Clotting

Pickering, "Modern Conceptions of Blood Clotting," *Brit. Journ. Exper. Biol.,* 1925, 2.

INDEX

Abdominal wall, rigidity of, in inflammation, reflexes controlling, 41
Acapnia, 7
  in anæsthesia, 149, 340
  prevention of, 128, 340
  shock, 125, 128, 149
Accommodation, muscle of, 75
  reaction of, 82
Achalasia and spasm of pylorus, diagnosis between, 237
Achondroplasia, 215
Acidosis, causes of, 249, 269
  increased ammonia excretion in, 263
  pregnancy, causes of, 334
  reaction of urine in, 260
  reduction of blood alkali mistaken for, 269
Acromegaly, pituitary in relation to, 214
Adaptation, structural, endocrines in relation to, 328
Addison's disease, colour of skin in, 317
Adenoids, anoxæmia in, 149
  obstruction to Eustachian tube in, 84
Adiposis dolorosa genitalis, pituitary in relation to, 215
Adiposity and gelatinoid degeneration of subcutaneous tissues, diagnosis between, 318
  lack of exercise in relation to, 301
Adrenaline, action of, 324
  in treatment of asthma, 324
Adystrophies, muscle reflexes in, 17
Afferent projection system in speech, 53
After-nystagmus, production of, 50
Agglutination tests of blood, 129
Agglutinins in protection against disease, 313
Air-hunger in shock, 126
  quality of, in relation to respiration, 161
Alcohol, action of, on venous pressure in heart failure, 143
  and heat loss, 286, 288, 292
  as cause of flushed skin, 317
  beneficial effects of, at mealtime, 224
  effect of, in hot countries, 319
  influence on heart rate, 94
Alcoholic coma, cilio-spinal reflex in, 82
Alcoholism, chronic, thirst in relation to, 275
  loss of equilibrium in, causes of, 52
  loss of heat in, 284
Alimentary canal, secretion of, psychic influence on, 188
  suitability of food for, 188
  ulcers of, excessive muscular action due to, 240
Alkali reserve in maintenance of neutrality of blood, 269
Alkalosis, 269
Allen treatment of diabetes, 251
Altitudes, high, general respiratory adaptation of blood, 178
Alveolar air, replacement of, in breathing, 151
  vital capacity in relation to, 154
Alveolar carbon dioxide in relation to maintenance of body neutrality, 271
Amino-acids and metabolism, 202
  inhibitory effect on growth of bacteria, 187
Ammonia in urine, 263
Ammonia-urea ratio and changes in body neutrality, 263
Amyotrophic lateral sclerosis, disturbances of sensation in, 32
Anabolism, 321
Anæmias, blood volume in, 159
  cerebral, in concussion, 5
    in relation to sleep, 302
  faintness in, 8
  general respiratory, adaptation by circulation in, 178
  skin pallor in, 316
  varieties of blood cells found in, 134
Anæsthesia, constriction of pupils in, 82
  failure of respiratory centre in, 149
  loss of heat in, 284
Anaphylactic fever, 288
Anarthia, 58
Aneurysm affecting sympathetic nerve, 82
Ankle clonus, 39
Ankylostomiasis, eosinophilia in, 135
Anoxæmia, 167-173
  Bohr effect accentuating, 168
  cerebral, cause of epileptic fit, 8
  distinction from carbon dioxide retention, 168
  due to high altitudes, 168
  due to venous obstruction, effect on capillaries, 172
  effects on nervous system, 171
  general, symptoms of, 170

Anoxæmia, in adenoids, 149
in carbon monoxide poisoning, 167
in relation to œdema, 172, 276
local, 171
collateral circulation in relation to, 172
of blood-vessels, causes of, 278
stagnant type, 155, 167, 170
sudden, effects of, 171
types of, 168
Anti-neuritic vitamin, 200
Anti-rachitic food factor, 197
Anti-typhoid inoculation, rise in temperature following, 288
Antipyretics in fever, 291
Antitoxins, in protection against disease, 311
Anuria, causes of, 259
Aortic disease, faintness in, 8
incompetence, effect on pulse, 101
pressure, factors influencing, 337
failure of, 337, 338
stenosis, effect on pulse, 102
valve, disease of, effect on second sound of heart, 105
Aphasia, 53, 57
recovery from, 59
site of brain lesion causing, 58
varieties of, as disorders of symbolic thinking, 59
Apoplexy, injury to pyramidal tract in, 14
Appendicitis, pain in, 27
Appendicular abscess, increased heart rate in, significance of, 93
Appetite and hunger, differentiation of, 207
Aqueous humour, 73
Argyll-Robertson pupil, 80
Arms, motor areas for, in brain, 14
Arterial disease, effect on blood pressure, 114
Arteries, condition of, in shock, 126
contraction of, when punctured, 131
elasticity of, velocity of pulse wave dependent upon, 115
Arterioles, constriction of, effect on arterial pressure, 115
Arteriosclerosis, beaded and tortuous retinal arteries in, 77
constriction of arterioles in, 115
Arthritis deformans and occupation, relationship between, 216
Ascites in liver cirrhosis, treatment of, 279
removal of large quantity of fluid in, faintness following, causes of, 7
Asphyxia, increase of ammonium salts in urine, 270
stages of, 339
unconsciousness due to, 10
Association mechanisms in speech, 53
Astasia, 52
Asteriognosis due to lesions of parietal lobe, 56
Asthma, adrenaline in treatment of, 324
cyanosis and dyspnœa in, 165
eosinophilia in, 135
obstruction to respiratory passages in, 153
respiratory reflex concerned in, 182
treatment of, 166
Astigmatism, 73
Asynergia, 76
Atropine, action of, on parasympathetic, 325
administration of, thirst following, 220
effect on heart rate, 94
effect on sinus arrhythmia, 99
in pyloric spasm, 243
in spasm of large intestine, 230
instillation, action of, 81
Auditory meatus, external, 83
internal, lesions of, effects of, 87
nerve tumour, signs of, 89
Auricle, function of, 100
Auricular fibrillation, 100
mitral stenosis and, 100
Auricular flutter, 100
Auriculo-ventricular bundle, conductivity of, 97
Auriculo-ventricular murmurs, 103
Auscultation of heart beat, 90
Autonomic nervous system, 320-327
composition of, 320
in relation to exercise, 296
Awareness, state of, 66
Axon reflex, 35, 296

Babies, excessive loss of heat by, 292
Babinski's reflex, 38
Bacillus coli infections, diurnal variation of temperature in, 283
Bacteria, growth of, inhibitory effect of certain amino-acids on, 187
Bainbridge's reflex, 92
Bárámy's eye tests for vestibular function, 50
Basal ganglia, reflex from, governing expression of face, 19
Basal metabolic rate, 191
in hyperthyroidism and myxœdema, 192
Basophil leucocytes, 135
Bed exercises, value of, 296
Bed sores, prevention of, 317
Belladonna, effect on heart rate, 94
in urinary incontinence, 326
Bell's paralysis, 20
Beriberi, anæsthesia in, neuritic origin of, 31
causes of, 279
due to vitamin B deficiency, 200

Betz cells, commencement of motor movement at, 15
Bicarbonate injections in diabetes, 10
Bile, formation and excretion of, 253-256
  fractions of, 256
Bilious attack, causes of, 225, 239
Bilirubin, formation of, 253
Birth palsies, 17
Bladder, excessively full, emptying of, syncope following, 8
Blind spot, 76
Blood, agglutination tests for, 129
  anti-bacterial power of, in relation to temperature, 287
  as a respiratory tissue, 159
  "buffer" salts of, 267
  carbon dioxide in, analysis of alveolar air in estimation of, 271
  carriage of carbon dioxide by, 354
  carriage of oxygen by, 351
  clotting of, factors influencing, 131
  coagulation of, in arrest of hæmorrhage, 131
  colloidal clotting complex of, 131
  colorimetric estimation of hæmoglobin content of, 9
  compatibility of, tests for, 129
  corpuscles of, white, 134
  count, differential, 134
  general respiratory adaptations in, 178
  grouping, importance of, in skin-grafting, 130
  groups, 129
    influence of disease upon, 135
  histology of, 133-136
  in maintenance of body neutrality, 267
  in relation to skin colour, 317
  letting in treatment of acute heart failure, 142
  loss of, unconsciousness due to, 7
  maintenance of neutrality of, alkali reserve in, 269
    kidney and, 258, 269
    liver and, 269
  neutrality of, 160
  pooling of, in certain cases of fainting, 7
  pressure, 113-118
    adaptation of, to posture, 121
    effect of arterial disease on, 114
    effect of hæmorhage on, 122
    effect of shock upon, 123
    factors governing, 113
    function of, 113
    heart in relation to, 113
    high, proteins causing, 347
    measurement of, 113
Blood, pressure, peripheral resistance and elasticity of blood-vessels in relation to, 114
    pulse pressure, 117
    venous pressure, 118
    volume of blood in relation to, 114
  quality of, effect of high altitudes on, 10
    effect of inspired gases on, 9
    in relation to colour of skin, 317
    in relation to increased heart rate, 93
    in relation to unconsciousness, 8
  red corpuscles of, histology of, 133
  respiratory function of, 351
  salts and maintenance of body neutrality, 267
  sugar, increase of, causes of, 330
    normal level of, 246
  sugar and pancreatic efficiency, 246-252
  sugar curve, 247
  supply of cerebrum, maintenance of, 5
  temperature of, influence on sensitivity of respiratory centre, 148
  transfusion of, 129
    tests for compatibility, 129
  urea in relation to kidney efficiency, 262
  vessels, anoxæmia of, causes of, 278
    elasticity of, in relation to blood pressure, 114
    fluid retention of, mechanism of, 275
    power of closing of, in arrest of hæmorrhage, 130
  volume of, in anæmias, 159
    in relation to blood pressure, 114
    reduced in cholera, 123
    restoration of, method of, 338
Body, effect of cold on, 286
  fluids of, in relation to salt excretion, 280
  heat, loss of, causes and treatment of, 341
  iodine supply of, importance of, 203
  motor areas for, in brain, 15
  neutrality, changes in, ammonia-urea ratio and, 263
    maintenance of, 267-273
      exercise in, 299
      factors governing, 267
  overheating of, disease causing, 341
    symptoms and treatment of, 341
  protective mechanisms of, 308
  protein supply of, importance of, 203
  sugar uses by, 248
  temperature of, 283-292
  water content of, 274-282
    abnormal, 275
    general retention of, 275
  weight, 206-211
    and growth of infants, 210
    definition of, 206
    endocrines in relation to, 211, 331

Body, weight, energy intake and output in relation to, 206
factors influencing, 206
menopause in relation to, 334
pancreas in relation to, 331
starvation in relation to, 207
thyroid in relation to, 331
Bohr effect accentuating anoxæmia, 168
Boilermaker's deafness, 88
Bomb calorimeter, 185
Bone, growth of, influence of pituitary on, 214
Bones and joints in relation to voluntary movement, 18
Bowman's membrane, 72
Brain, and stomach, antagonism between, 244
cortex of, lesions of, effects of, 14
extra-pyramidal tracts of, 15
frontal lobes of, as higher motor area, 15
motor areas of, regions governed by, 14
in sequence of, in relation to blood supply, 15
oxygen requirements of, 9
pyramidal tracts of, 12
softening of, 15
special sense areas in, localization of, 56
speech areas in, localization of, 56
Breathing, 145-162
centre for, 145, 146
effects of interference with movements of diaphragm on, 152, 153
efficiency of, factors involved in, 162
mechanics of, 152
neutrality of blood in relation to, 160
patency of respiratory passages, 153
quality of air breathed, 161
replacement of alveolar air in, 151
respiratory surface, 149
shallow, fatigue in relation to, 149
production of, mechanism of, 147
Breathlessness and cyanosis, 163-167
in acute heart failure, 141
in relation to cardiac reserve, 139
oxygen want, 155, 163
in uræmia, nature of, 159
physiological, 146
Broca, area of, 15
Bromides, depressants of reflex action, 44
Bronchioles, function of, 166
Bronchitis, the "three milestones" of, 156
"Buffer" salts of blood, 267

Calcium deficiency in relation to vitamins, 199
Calculus in relation to fluid intake, 274
Calorific consumption of three normal individuals, 193-196
value of foods, 184
Canalization of reflexes, 39
Cancer of intestines, excessive peristalsis in, 230
Capillaries, enormous dilatation of, treatment of, 338
nervous control of, 278
Carbohydrate metabolism, 343
deficient, 246
pancreas in, 330, 331
Carbohydrates, calorific value of, 185
classification of, 343
Carbon dioxide, alveolar, in relation to maintenance of body neutrality, 271
carriage of, by blood, 354
in blood, method of estimation of, 271
Carbon monoxide, inspired, effect on blood, 9
poisoning, anoxæmia in, 167
Cardiac disease, chronic venous congestion in, cyanosis accompanying, 165
exercise in, 297
efficiency and disease, physiological principles in relation to, 137-144
venous pressure as index of, 276
failure, œdema in, 276
primary, causes of, 334
massage in, 337
œdema, treatment of, 279
reserve, 138
Cardio-spasm, causes of, 219
Carotids, compression of, causing unconsciousness, 6
Carriers, treatment of, 313
Cataract, 74
Catheterization in dye excretion from ureter, 265
Cavernous sinus, thrombosis of, œdema in, 278
Central nervous system, lesions causing shock, 124
paths of impulses from viscera into, 26
Cerebellar tumour, symptoms of, 6
unconsciousness, 6
Cerebellum and mid-brain, in relation to equilibrium, 51
Cerebral anæmia in concussion, 5
Cerebral artery, middle, blockage of, effects of, 14
Cerebral circulation, effect of general circulatory failure on, 157, 158
Cerebral compression, symptoms of, 5
Cerebral injury, cerebral circulation in relation to, 158
Cerebral tumour, optic neuritis in, 77
unconsciousness in, 6
Cerebrum, blood supply of, maintenance of, 5

Cervical rib, paralysis of sympathetic nerve from, 82
Chemiotaxis, 134
Chlorosis, blood volume in, 159
increased heart rate in, 93
Cholera, appearance of blood in cases of, 123
facial expression in, 20
hypertonic saline treatment of, 274
in relation to fluid intake, 274
Chorda tympani and salivary digestion, 220
Chorea, movements of, origin of causes of, 15
Choroiditis, pale areas in, 77
Cilio-spinal reflex, 82
Circulation, action of sympathetic and parasympathetic on, 321
effect of exercise on, 297
effect of shock on, 126
general respiratory adaptations in, 177
integration of, 119-123
pulmonary, 154
Circulatory conditions affecting consciousness, 6
Cirrhosis of liver, ascites in, treatment of, 279
œdema as symptom of, 278
Clothing and body temperature, 287
Coagulation of blood in arrest of hæmorrhage, 131
Cocaine poisoning, constriction of pupils in, 82
Cochlea, canals of, pathological changes in, 88
Cold, sensation of, 22
Cold bath, effect of, on body, 286
in high fever, effects of, 290
Colds, treatment of, 318
Colic, and inflammatory lesions of intestines, diagnosis between, 230
movements of intestine in, 230
pain of, intermittent nature of, 27
treatment of, 230
Colitis, treatment of, 231
Coma, extensor reflex present in, 39
Complex, definition of, 68
Compression, medullary, commencing, symptoms of, 6
of carotids causing unconsciousness, 6
Concussion, 5
Conditioned reflexes, 41, 43
causing hunger contraction, 208
Conjunctival reflex, 88
Consciousness, 5-11
conditioned reflexes and, 43
elimination of toxic substances and, 10
maintenance of blood supply in relation to, 5
Consciousness, physical integrity of cerebrum in, 5
quality of blood in, 9
Constipation, 230
deficiency of fluid intake as cause of, 190
Cooking, effect on vitamins, 198
importance of, 343
Co-ordination, defects of, results of, 50, 52
impulses governing, 30
of voluntary movement, 44
Cor bovinum, production of, 105
Cornea, composition of, 72
conical, 73
normal curvature of, alterations affecting vision, 73
ulcers of, impairment of vision in, 73
Corpuscles, corneal, 72
formation, stimulus to, 133
red, breaking down of, 134
histology of, 133
Corrigan pulse, 102
Cortex, of brain, lesions of, effects of, 14
Cough, respiratory reflexes concerned in, 181
Cranio-sacral autonomic group of nerves, 320
Creatinine in urine, 263
Cretinism, causes of, 213
Cyanosis, accompanying chronic venous congestion in cardiac disease, 165
and breathlessness, 163-166
in acute heart failure, 141
in cerebral compression, 6
late, in pneumonia, causes of, 164, 165
Cyclitis, impairment of vision in, 73
Cystoscope in dye excretion from ureter, 265

Deafness, boilermaker's, 88
internal ear, 87
middle ear, 84
Rinné's test in, 86
Weber's test in, 86
senile, 88
Decerebrate rigidity, 15
Degeneration, of lenticular nucleus, facial expression in, 19
reaction of, 17
Depressor reflex, influence on integrity of circulation, 120
Descemet's membrane, 72
Desires and instincts, antagonism between, 63
Dextrin, 223
Diabetes, abnormal acids in blood in, 272
bicarbonate injections and insulin therapy in, 10
carbohydrate metabolism in, 211, 252
complications of, cause of, 314
diagnosis of, 247

Diabetes, excess of fat in stools in, 206
exercise in, effects of, 297
fat metabolism in relation to, 346
insipidus, polyuria as symptom of, 259
mellitus, experimental production of, 247
mental anxiety as cause of, 248
pancreas and thyroid in relation to, 332
pancreatic efficiency in relation to, 249
treatment of, by Allen method, 251
by diet, 247
by insulin, 250
dangers of, 251
Diabetic coma, prevention of, 252
value of insulin in, 251, 252
Diaphragm, movements of, interference with, effects on breathing, 152
Diaphragmatic pain, referred to fifth cervical segment, 25
Diarrhœa in relation to fluid intake, 274
lienteric, causation of, 207
Diastase in urine, 265
Diet, and growth, 212
in relation to intestinal movements, 231
influence on urinary reaction, 261
protein constituents in, 185
salt content of, 190
Dietaries, average, caloric value of, 185
Digestion, action of parasympathetic and sympathetic on, 321
and swallowing, 218-228
in maintenance of body neutrality, 267
protein, in stomach, 221
salivary, factors influencing, 220
in stomach, 227
Digestive organs, effect of exercise on, 299
Digestive secretions, in protection against disease, 309
Digitalis, in treatment of heart failure, 143
Diphtheria, cardiac failure in, 137
Schick test in, 312
Disease, protection against, 308-314
agglutinins in, 313
antitoxins in, 311
body temperature in, 314
immune bodies in, 310
kidney in, 310
lysins in, 310
metabolism in, 314
mucous membrane in, 308
opsonins in, 311
oxygen supply in, 314
precipitins in, 313
reticulo-endothelial system in, 310
skin in, 308
Disseminated paralysis, organic and functional paralysis in, 19
sclerosis, disturbances of sensation in, 32
rotating nystagmus in, 51
Dizziness, 8
due to sudden alteration of posture, causes of, 121
Dreams, analysis of, 69
in psychoneuroses, 70
Drop-foot, 18
Drop-wrist, 18
Drowning, treatment of, 340
Drugs, action of, in relation to reflexes, 44
administration of, causing leucocytosis, 135
therapy in heart failure, 143
to stimulate kidney in œdema, 282
sweating, 281
used in circulatory collapse, 338
Duodenal ulcer, localized irritation in, 239
Dwarfism, pituitary in relation to, 214
Dyes, excretion of, in urine, 265
Dysentery, acute, tenesmus in, 240
movements of intestine in, 229
treatment of, 230
ulcer following diagnostic sign of, 240
Dyspepsia, flushed skin in, 317
Dysphagia, causes of, 218
Dyspnœa, 163-167
and cyanosis in asthma, 165
in uræmia, effect of reduction of pressure of cerebro-spinal fluid in, 10
physiological, 146
Dystrophies, muscular, 17

Ear, auricle of, 83
external, 83
internal, 87
middle, 84
nervous pathways of, 88
ossicles of, 85
oval window of, pathological changes in, 87
semicircular canals of, function of, 50
Effector mechanisms in speech, 57
Efferent projection mechanism in speech, 57
Eighth nerve, lesions of, effects of, 89
Einthoven's string galvanometer, 110
Electricity, effects of, 296
Electrocardiograph, 110
leads of, 110
Embolism, skin pallor in, 316
sources of, 15
Emergencies, physiological principles in treatment of, 336-342
Emotions, effect of, on endocrines, 329
on salivary secretion, 220
Emphysema, compensatory, 150, 177
effect of increased pulmonary resistance in, 155
increased lung surface in, 151

Empyema, causes of, 278
Encephalitis lethargica, generalized hypertonus in, 39
Endocrine organs, and growth, 213
balance of, 328-335
in pregnancy, 330, 333
Endocrine organs, balance of, in relation to body weight, 211, 331
to disease, 330
table showing, 328
effect of emotions on, 329
in relation to adaptation, 328
Endocrinology, hypotheses of, 328
Energy, intake and output, in relation to body weight, 206
supply in relation to feeding, 184
Enterosympathetic group of nerves, 320
Eosinophil leucocytes, granular, 135
Eosinophilia, associated with parasitic affections, 135
in ankylostomiasis, 135
in asthma, 135
Epilepsy, spasm of retina in, 76
Epileptic fit, symptom-complex of, 8
Equilibrium, 48-52
cerebellum and mid-brain and, 51
function of eye in relation to, 48
loss of, in alcoholism, causes of, 52
in unconsciousness, causes of, 52
muscle sense in relation to, 49
Romberg's sign in, 49
vestibular apparatus in relation to, 49
Erect posture and intestinal stasis, 231, 233
Erythrocyte, 133
Eserine, use of, effects of, 81
Eustachian tube, 84
Ewald test meal, 225
Exanthemata, distribution of rash in, 316
fever in relation to, 290
Exercise, and rest, 293-307
anticipation of, increased blood pressure in, 116
cardiac disease and, 297
cardiac reserve and, 139
circulation and, 92, 297
diabetes and, 297
digestive organs and, 299
excessive, condition of urine following, 261
muscular fatigue in, 295
flushed skin in, 316
gradual, in later treatment of heart failure, 142
ideal, 295
in relation to disease, 294
metabolism, 299
vitamin deficiency, 199
Exercise, lack of, effect of, 300-302
maintenance of body neutrality, 267, 299
mental effects of, 299
muscles and, 294
muscular, and body heat, 286
effects of, 321
nervous system and, 298
relation to autonomic nervous system, 296, 298
respiration and, 298
sudden, effect on heart, 139
vagal and vaso-motor tone and, 298
Exhaustion, from exposure, feeding in, care necessary, 341
Exophthalmic goitre, facial expression in, 19
increased heart rate in, causes of, 94
Exposure, death from, causes of, 341
Expression, associations connected with area in brains responsible for, 56
facial, basal ganglia in relation to, 19
physiology of, 19
External auditory meatus, obstructions in, 84
Extra-pyramidal tracts of brain, 16
Eye, aqueous humour of, 73
movement and reflexes of, 72-82
normal tension of, 73
reflexes of, 78
reaction of accommodation, 82
vitreous humour of, 74
Eyes, function of, in relation to equilibrium, 48
movements of, relationships of semicircular canals to, 50

Face, expression of, eyes in relation to, 19
in lenticular degeneration, 19
in Parkinson's disease, 19
motor areas for, in brain, 15
movements of, 19
muscles of, innervation of, 20
Facial nerve, lesions of, effects of, 20, 89
Facies Hippocratica, 20
Fainting, certain cases of, pooling of blood in, 7
fits, method of production, 7, 8
treatment of, 8
Faintness, 8
Fasting, value of, 208
Fat metabolism, 345
Fatigue, causes of, 302
in relation to rapid and shallow breathing, 149
industrial, treatment of, 305
muscular, 294
treatment of, 304

Fats, caloric value of, 185
causing goitre in animals, 204
Feeding, in exhaustion following exposure, care necessary, 341
physiological principles in, 184-196
energy supply and tissue repair, 184
food and calorific consumption of three normal individuals, 193-196
suitability of food for alimentary canal, 188
sunlight in relation to, 189
vitamin content of food in, 188
water and salts in, 190
Fever, anaphylactic, 289
antipyretics in, 291
carbohydrate diet in, value of, 288
causes of, 288
flushed skin in, 316
increased heart rate in, causes of, 93
significance of faintness of first heart sound in, 103
Fibrinogen-prothrombin complex, 131
Fingers, clubbing of, in chronic pulmonary conditions, 215
Fistula, intestinal, reverse peristalsis in, 228
Fœtus, at seventh month, degree of development of, 1
evidence of separate existence, 2
growth of, 1
Food, and calorific consumption of three normal individuals, 193-196
calorific value of, 185
chemical nature of, in relation to gastric juice, 222
energy value of, 184
importance of cooking of, and digestion, 224
physical state of, importance of, 188
suitability of, for alimentary canal, 188
vitamins in, 188, 197-200
Foreconscious, 67
Forgetfulness, 293
Fractures, massage and movement in, importance of, 296
Free association method in psycho-analysis, 301
Friedreich's disease, disturbances of sensation in, 32
Frontal lobes of brain as higher motor area, 15
Fruits, beneficial effects of, 189
Functional paralysis, 18

Gallstones, referred pain in, 25
Gas poisoning, effect on oxygen in blood, 10
Gastrectomy, partial, 240
Gastric ailments, common, physiological and pharmacological principles in relation to, 236-245
atony, 238
contents, acidity of, control of, 224
investigation of by test meal, 225
function in relation to gastric symptoms, 245
irritation, 239
juice, secretion of, factors influencing, 221
in relation to chemical nature of food, 222
pain, causes of, 26, 236
ulcer, as cause of starvation, 207
dietetic treatment of, 242
localized irritation in, 239
medical treatment of, 242
surgical treatment of, 240
Gastrin, action of, 223
Gastritis, acute, general irritation in, 239
Gastro-enterostomy, 240
General paralysis, absence of light reflex in, 80
Gigantism, pituitary in relation to, 214
Glaucoma, 74, 77, 78
pilocarpine in, 327
Glycosuria, causes of, 330
in pregnancy, 333
renal, cause of, 246
Goitre, a water-borne disease, 204
endemic, excessive calcium causing, 204
iodine administration in, 204
exophthalmic, in relation to thyroid and pancreas, 202, 331
simple, and iodine deficiency, 190, 203
Gout, purine metabolism in relation to, 348
urates in, 264
Grafts of ductless glands, importance of blood grouping in, 130
Growth, 212-216
diet in relation to, 212
diseases affecting, 213
effect of thyroid deficiency on, 214
light in relation to, 213
local, 215
pituitary in relation to, 214
thyroid in relation to, 202, 213
vitamins in relation to, 213
Gum infusions in treatment of shock, 127

Habit formation, conditioned reflexes and, 43
psychology of, 61
Hæmoglobin content of blood, colorimetric estimation of, 9
Hæmoglobinometer, use of, 9

Hæmophilia, 132
Hæmorrhage, and allied conditions, effect of, 122
arrest of, 130
in shock, 126
post-partum, uterine massage in, 337
skin pallor in, 315
treatment of, 337
Hæmorrhoids, skin pallor in, 316
Haldane's oxygen apparatus, 174
Hearing, 83-89
associations of areas in brain responsible for, 56
Heart, auriculo-ventriculo bundle, conductivity of, 97
chambers of, hypertrophy of, shown by electrocardiograms, 111
control of, nervous mechanism of, 92
dilated, effect on first heart sounds, 103
disease, congenital, general respiratory adaptation of blood in, 179
effect of sudden exercise on, 139
efficiency of, and disease, physiological principles in relation to, 137-144
failure, acute, drug therapy in, 143
symptoms of, 141
treatment of, 141
in diphtheria, 137
fatty degeneration and infiltration of, 137
function of pericardium, 139
impairment of, effect of, on rate, 94
in relation to blood pressure, 113
increase in rate of, mechanisms governing, 90
innervation of, 91
"law of the," 91, 137
-lung preparation, 91
mammalian, properties of, 2
muscle, hypertrophied, effect on first heart sound, 103
musculature of, in relation to efficiency, 137
of frog, properties of muscle of, 2
output of, factors governing, 91
power of, to respond to increased demands, 137
reserve capacity of, 138
right ventricular failure, in pneumonia, causing late cyanosis, 165
sounds, character of, 102-106
first sound, significance of, 102-104
second sound, 104
stimulation of, by substances ingested, 94
the rate of, 90-95
Bainbridge's reflex in, 92
Heart-block, causes of, 98
intermittent, 98
recognition of, 98
Heart rate, atropine and, 94
belladonna and, 94
excessive, quality of blood in relation to, 93
exercise and, 93
increased, due to alcohol, 94
in appendicular abscess, significance of, 93
in chlorosis, 93
in exophthalmic goitre, causes of, 94
in fever, causes of, 93
significance of, 94, 95
nicotine and, 94
pain and, 92
pulse pressure dependent upon, 117
slow, in myxœdema, 94
under both nervous and chemical control, 90
Heat, diminished loss of, in fever, mechanism of, 289
local, and body temperature, 287
loss of, 285
production of, by muscles, 284
regulating centre, 284
sensation of, 22
stroke, causes of, 285
Hemiplegia, increased muscle tonus in, 39
supra-nuclear lesions in, 21
Heredity in relation to originality, 64
Hering-Breuer Reflex, 147
Herpes, in locomotor ataxia, 278
zoster, blebs of, 278
High altitudes, effect on quality of blood, 10
Histamine, absorption of, by alimentary canal, 317
action of, 223, 325
shock, 124, 284
Hodgkin's disease, œdema in, 278
Hot baths, fainting in, causes of, 8
Hunger and appetite, differentiation of, 207
pain, 207
striking, effect of, 208
Hydrarthrosis, intermittent, 278
Hydrochloric acid in relation to ulcer, 240
Hydrogen ion concentration, 349
compatible to life, 267
determination of, 350
indicators for, 351
of body fluids, alterations of, 267
of urine, 260
Hyperæsthesia, 33
Hyperchlorhydria, in relation to pyloric contraction, 237
Hyperglycæmia, causes of, 247
Hypermetropia, 75
Hypersecretion of stomach, 237

Hyperthyroidism, and high metabolic rate from emotion, diagnosis between, 329
basal metabolic rate in, 192
heart in, 204
iodine in treatment of, 205
signs of, 204
treatment of, 205,
Hypnosis in psycho-therapy, 70
Hypochondriasis, spasm of sphincter in, 219
Hypothyroidism and iodine deficiency, 203
Hysteria, absence of conjunctival reflex in, 80
sensory changes in, 32
shallow breathing in, 147
spasm of sphincter in, 219
Hysterical paralysis, 18

Ileo-colic reflex, 233
Immune bodies in protection against disease, 310
Immunity, active and passive, 311
non-sterilizing, 313
Impulses, paths of, from viscera into central nervous system, 26
Indigestion, causes of, 237, 344
ptyalin, 188
symptoms of, caused by pyloric spasm, 26
Infant feeding, physiological principles in, 210
Infants, body weight and growth of, 209
pulse rate in, 90
Infection, body temperature in relation to, 286
Inflammation, characteristics of, 309
Innervation, of ear, 88
of eye, 79, 81
of facial muscles, 20
of heart, 91
of striped muscle, 12
of tongue, 21
reciprocal, principle of, 41
Instincts and desires, antagonism between, 64
Insulin, in diabetic coma, value of, 251
dangers of, 251
standardization of, 246
treatment of diabetes, 10, 251
Integration of the circulation, 119-122
Interest, necessity for, 302, 305
Internal ear, 87
Interstitial keratitis, impairment of vision in, 73
Intestinal stasis, 230
anastomosis in, 232
and chronic nephritis, relationship of, 235
diagnosis of, 234
Intestinal stasis, liquid paraffin in, 231
X-ray diagnosis of, 234
Intestine, general respiratory adaptation by, 179
large, spasm of, causes of pain in, 230
treatment of, 231
"law of the," 230
movements of, 229-235
diet in relation to, 232
phosphates in relation to, 231
obstruction of, excessive peristalsis in, 230
Intestines and maintenance of body neutrality, 267, 270
Intoxications, influence of, on growth, 213
Intra-ocular pressure, 73
tympanic pressure, regulation of, 86
Iodine, deficiency of, goitre due to, 190
in relation to thyroid, 203
in treatment of hyperthyroidism, 205
supply of body, importance of, 203
Iridectomy in glaucoma, 74
Irritation, gastric, 239
Islets of Langerhans and sugar utilization, 248

Jaundice, varieties of, 253-255
Jaw, jerk of, 39
muscles moving, lesions of, 21
Jejunostomy, 240
Joint and muscle sense, 29
Joints and bones, in relation to voluntary movements, 18
Jordan's band, 231
"Juxta-pyloric" ulcers, 239

Katabolism, 321
Keith-Flack node of heart, 97
Keratitis punctata, 73
Ketosis, cause of, 250
Kidneys, anatomy of, 257
and maintenance of body neutrality, 267, 269
diseases of, ammonia excretion and, 263
creatinine excretion and, 263
excretion by skin in, 318
urea formation and, 262
elimination of bacteria from blood-stream by, 310
functions of, 258
general respiratory adaptation by, 201
leak points of, 246
nervous control of, 260
secretion of urine by, opinions on, 257
stimulation of, in œdema, 282
Knee jerks, 36

Labour, onset of, pituitary hormone causing, 333
Labyrinthine disease, loss of equilibrium due to, 50
Lane's kink, 231
"Law of the heart," 138
"Law of the intestine," 230
Legs, motor areas for, in brain, 14
  reflexes of, 36
Lens, the, 74
Lenticular degeneration, facial expression in, 19
  increase of reflexes and tone in, 16
Lenticulo-striate artery, rupture of, in apoplexy, 14
Leontiasis ossia, 215
Leucocytes, differentiation of, 135
Leucocytosis, 136
Leukæmia, blood conditions in, 136
Light, and growth, 213
  reflex, 80
Liver, and maintenance of body neutrality, 267, 269
  cirrhosis of, ascites in, treatment of, 279
    œdema as symptom of, 277
  function of, in digestion, 344
  general respiratory adaptation by, 179
Locomotor ataxia, herpes and œdema in, 279
Loewi's test, 82
Lovén reflexes, 35, 296
Lungs, circulation in, 154
  collapse of, causes of, 150
  diminution of surface of, 150
  general respiratory adaptations in, 176
  nature of respiration in, 149
  normal circumference of, 150
  replacement of alveolar air in, 151
Lymph glands, rôle of, in protection against disease, 309
Lymphocytes, histology of, 134
Lysins, in protection against disease, 310

Malaria, causes of, 288
  lymphocytosis in, 135
  symptoms of, 289
Mammalian heart, properties of, 2
Marasmus, 215
"Masque tabetique" of Duchenne, 31
Massage, effects of, 296
Mastication, importance of, 219
Medullary compression, commencing symptoms of, 6
Megaloblasts, 134
Meissner's corpuscles, 23
Ménière's disease, vertigo in, due to labyrinthine disease, 50
Menopause, in relation to body weight, 334
Mental attitude, in sensation, 32
Mental rest, state of, in estimation of basal metabolic rate, 191
Metabolism, amino-acids and, 202
  basal, 185, 191-193
    increased, in treatment of obesity, 209
    thyroid in, 331
  carbohydrate, 343
    deficient, 246, 250
    in diabetes, 211
    pancreas in, 329-332
  exercise in relation to, 299
  fat, 345
  in maintenance of body neutrality, 267
  in protection against disease, 314
  in relation to temperature, 283
  influence of internal secretions on, 211
  influence of nervous system on, 192
  protein, 346
  purine, 348
  stimulating effects of protein on, 186
  thyroid in relation to, 202, 213, 329
Methemoglobinæmia, colour of skin in, 317
Middle ear deafness, 85
  Rinné's test in, 86
  Weber's test in, 86
Milk, pasteurization of, effect on vitamin content, 198, 201
Mind, primary and secondary systems of, 67
Mitral stenosis, auricular fibrillation in, 100
Mitral valve, impairment of, effect on pulmonary circulation, 156
    murmur due to, 103
Monotony, effect of, 302, 304, 305
  relief of, 306
Moro's tuberculin ointment in diagnosis of tuberculosis, 312
Morphia, in spasm of large intestine, 230
  in treatment of heart failure, 143
Motor functions, psychology of, 61
Motor movement, commencement of, at Betz cells, 15
Movement, voluntary, 12-21
Movements and reflexes, of eye, 72-82
  of face, 19
  of the subconscious, 60
  of voluntary muscle, 15
  reflex, 35-47
  voluntary, bones and joints in relation to, 18
    hysterical paralysis and, 18
Mucous membrane in protection against disease, 299

Murmurs, auriculo-ventricular, 103
cardiac, causation of, 104
in pericarditis, 106
presystolic, 106
systolic, 103, 104
Muscle, and joint sense, 29
of accommodation, 75
pain in, cause of, 23
sense, from facial muscles, course of, 20
in relation to equilibrium, 49
sensations, unconscious, pathway of, 29
spasm of, gastric pain caused by, 26
tone, loss of, with disappearance of spinal reflex, 37
reduction of, in relation to temperature, 284
Muscles, degeneration of, 17
effect of exercise on, 294
in acute poliomyelitis, condition of, 17
in pseudo-hypertrophic paralysis, condition of, 17
interference of motor path of, results of, 17
moving jaw, paralysis of, 21
paralysis of, 17
place of, in heat production, 284
reaction of degeneration of, 17
spasm or rigidity of, 17
striped, control of, 12
voluntary, movements of, 15
Muscular adaptation, 295
Muscular dystrophies, absence of spinal reflex in, 36
Muscular fatigue, 294
Myocarditis, chronic, 156
heart efficiency in, 137
Myocardium, primary disease of, 156
Myopia, 74, 75
Myxœdema, and iodine deficiency, 203
basal metabolic rate in, 192
causes of, 329
heart rate slow in, 94
pancreas and thyroid in relation to, 332
subnormal temperature in, 292
thyroid and, 202
thyroid extract in, 213

Nasopharyngeal neoplasm, obstruction to Eustachian tube in, 84
Nephritis, acute, blood urea in, 263
œdema in, 275
chronic, and intestinal stasis, relationship of, 235
polyuria in, 258
interstitial, chronic, "head" of urea in, 262
skin pallor in, 316
retention of acid phosphate in, 269
Nerve endings, special, 22
Nerve paths, interference with, effect on sensations, 30
Nerves, sympathetic and parasympathetic, and salivary digestion, 220
Nervous control of capillaries, 279
Nervous mechanisms controlling respiratory centre, 146
Nervous system, autonomic, 320-327
effects of anoxæmia on, 171
effects of exercise on, 298
influence of, in metabolism, 192
Neurasthenia, exaggeration of reflexes in, 192
shallow breathing in, 147
under-eating associated with, 208
Neuritis, absence of spinal reflex in, 36
and neuralgia, œdema of, 278
numbness after, 31
under-eating associated with, 208
Neutrophil leucocytes, 135
Nicotine, action of, on heart rate, 94
on sympathetic-parasympathetic balance, 327
Nose, operations on, effects of on swallowing, 218
Nystagmus, production of, 50
rotating, causes of, 51

Obesity, causes of, 208
hormone therapy of, 209
thyroid treatment of, dangers of, 209
treatment of, 208
Œdema, and gelatinoid degeneration of subcutaneous tissues, diagnosis between, 318
angio-neurotic, 278
anoxæmia in relation to, 172
cardiac, causes of, 277
causes of, 275
in cardiac failure, 277
in Hodgkin's disease, 278
in locomotor ataxia, 278
in neuritis or neuralgia, 278
in thrombosis of cavernous sinus, 278
sign of pitting in, 276
skin pallor in, 316
toxins causing, 278
treatment of, 279
by drug stimulation of kidneys, 282
by heat, 281
by lowering salt content of diet, 280
by purgatives, 282
operative, 280
Œsophagus, obstruction of, 218
sphincter of, spasm of, 219
stricture of, as cause of starvation, 207

Oligæmia, 126
Opacities, corneal, 73
Open-air life, effects of, 293
Ophthalmoscope, use of, 76
Opium poisoning, constriction of pupils in, 82
Opsonic index, 311
Opsonins in protection against disease, 311
Optic disc, 76, 77
Optic neuritis in cerebral tumour, 77
Originality, influence of environment and tradition on, 64
Ossicles of ear, 85
Osteomalacia, 215
Otolithic cavities, function of, 49
Otosclerosis, 88
Over-eating, effects of, 208, 266
Oxaluria, treatment of, 265
Oxygen, apparatus, 173-175
  carriage of, by blood, 351
  in blood, effect of gas poisoning on, 9
  inhibiting effect on pneumococcus, 174
  requirement of brain, 9
  response of respiratory centre to, 158
  supply in protection against disease, 314
  therapy, 173-175
    methods of, 174
  want, breathlessness in relation to, 163

Paget's disease, 215
Pain, cardiac, in acute heart failure, 141
  effect on heart rate, 92
  gastric, causes of, 236
    muscular, origin of, 226
  in appendicitis, 27
  muscle, cause of, 23
  referred, 24
  relation to voluntary movements, 18
  sense of, 23
Palate, anæsthesia of, absence of conjunctival reflex in, 80
Palpitation, in acute heart failure, 141
Pancreas, and thyroid, antagonism between, 332
  function of, 329, 330
  in relation to body weight, 330, 331
  in relation to carbohydrate metabolism, 329, 330
Pancreatic disease, excess of fat in stools sign of, 206
  efficiency and blood-sugar, 246-252
    in relation to diabetes, 249
  inefficiency, causes of, 330
Paracusis in otosclerosis, 88
Paralysis agitans, degeneration of basal ganglia region in, 16
Paralysis agitans, bulbar, effect of on swallowing, 218
  causes of, 13
  crossed, 13
  functional, 19
  hysterical, 18
  of lower motor neurone, 13
  of muscles moving jaw, 21
  of stapedius muscle, 21
  of sympathetic nerve, 81
  of voluntary movement, 12
Parasites, presence of, eosinophilia associated with, 135
Parasympathetic group of nerves, 320
  atropine and, 325
  circulation and, 321
  digestion and, 321
  function of, 320
  nicotine and, 327
  pilocarpine and, 326
Parkinson's disease, facial expression in, 19
Pasteurization, effect on vitamins, 198, 201
Peptone, 223
Pericarditis, murmurs in, 106
Pericardium, dilatation of, physiological and pathological, 140
Perimeter, use of, 78
Peripheral failure in shock, 123
Peripheral resistance, alteration of, in hæmorrhage, 122
  in relation to blood pressure, 114
  variation in, according to locality, 116
Peristalsis, excessive, causes of, 229
Peristaltic waves, mechanism of, 227
Pernicious anæmia, diminution of red corpuscles in, 133
Persuasion on psycho-therapy, 69
Petechial hæmorrhages in concussion, 5
Petit mal, 8
Peyer's patches, rôle of, 309
Phagocytosis, 134
Phenolsulphonephthalein test, 265
Phosphates in relation to intestinal movements, 231
Phosphaturia, 264
Pilocarpine, action of on parasympathetic, 326
  use of, effects of, 81
von Pirquet's test in diagnosis of tuberculosis, 312
Pituitary, enlargement of, in pregnancy, 333
    thyroidectomy as cause of, 332
  in relation to adaptation, 329
  in relation to growth, 214
  in relation to onset of labour, 333
  in relation to urinary secretion, 259
  relationship of with thyroid, 332
Plantar protective reflex, 38

Plantar reflexes, two varieties of, 38
Pleurisy, shallow breathing in, 147
with effusion, respiratory distress small in, 164
Pleurodynia, referred pain in, 26
Pneumococcus effect of oxygen on, 174, 175
Pneumonia, chloride retention in urine in, 280
crisis of, 291
cyanosis and breathlessness in, 164, 165
hypostatic, 277
oxygen therapy in, 174
shallow breathing in, 147
subnormal temperature in, 292
Pneumothorax, shallow breathing in, 147
Poikilocytes, 134
Poisoning, chronic, with dyes or metals, colour of skin in, 317
with diarrhœa, in relation to fluid intake, 374
Poliomyelitis, acute, absence of spinal reflex in, 36
condition of muscles in, 17
anterior, acute, paralysis of lower motor neurone in, 13
limbs loose and flail-like after, 17
Polycythæmia, flushed skin in, causes of, 317
Polygraphs, use of, 107
waves of, 108, 109
Polymorpho-leucocytosis, significance of, 135
Polymorpho-nuclear leucocytes, 134
Polyuria, 258
as symptom of diabetes insipidus, 259
causes of, 249
in chronic nephritis, 258
Pons, lesions of, effect of, localization by, 89
Posture, adaptation of blood pressure to, 121
impulses governing, 29, 30
maintenance of, spinal reflex and, 37
Postural reflexes and co-ordination, 44
inherited, 45
Precipitins, in protection against disease, 313
Pregnancy, acidosis of, causes of, 334
endocrine balance in, 331, 334
enlargement of pituitary in, 334
extra-uterine, ruptured, skin pallor in, 315
glycosuria, 248, 334
Presbyopia, 75
Pressure, sense of, 22
Presystolic murmurs, 106
Progressive muscular atrophy, absence of spinal reflex in, 36
paralysis of lower motor neurone in, 13
Proprioceptive stimuli, 44
Proteins, as cause of high blood pressure, 347
Proteins, caloric value of, 185
composition of, 184
constituents in diet, 185
digestion in stomach, 221
irreducible minimum, 184
metabolism, endogenous, 348
exogenous, 346
requirements of body, 184
stimulating effects in metabolism, 185
supply of body, importance of, 203
Pseudo-hypertrophic paralysis, 17
Psychic influence on alimentary secretion, 189
Psychic secretion, 221
Psycho-analysis, 68
Psycho-galvanic reflex, 116
Psychology, and psycho-therapeutics, physiological aspects of, 60-71
new, in relation to therapeutics, 65
principles of, 66
of habit formation, 61
of motor functions, 61
of speech, 62
of thought, 62
Psycho-neuroses, dreams in, 69
Psycho-therapeutics and psychology, physiological aspects of, 60-71
Psycho-therapy, aims of, 68, 69
analysis of dreams in, 69
hypnosis in, 70
persuasion in, 69
suggestion in, 69
Ptosis, 79
Ptyalin indigestion, 189
secretion of, 220
Pulmonary circulation, 154-157
Pulse, and the heart sounds, 96-106
character of, 101
pressure, 117
dependent upon heart rate, 117
rate of, 90, 96, 97
in auricular flutter, 100
slow, in commencing medullary compression, 6, 7
"thready" or "running," 102
venous, 107-110
water-hammer, 102
wave, velocity of, dependent upon elasticity of arteries, 115
"wiry," 102
Pupils, constriction of, causes of, 81
dilatation of, causes of, 81
in severe exercise, 321
in shock, 126
inequality of, significance of, 82
innervation of, 81
Purine metabolism, 348
Pyæmia, symptoms of, 289

Pylorus, spasm of, and achalasia, diagnosis between, 237
atropine in, 243
symptoms of indigestion caused by, 26
Pyramidal disease, effects on reflexes, 38
Pyramidal tract, injury to, in apoplexy, 14
of brain, 13

Reaction, of accommodation, 82
of degeneration, 17
Receptive association areas of brain, lesions of, results of, 58
Receptor mechanisms in speech, 53
Reciprocal innervation, principle of, 40
Red blood corpuscles, histology of, 133
Referred pain, 24
Reflex, axon, 35, 296
Bainbridge's, 92
cilio-spinal, 82
conjunctival, 79
Hering-Breur, 147
ileo-colic, 233
light, 80
Lovén, 35, 296
movements, 35-47
phenomena, grades of, 60
postural, co-ordination and, 44
psycho-galvanic, 116
spinal, 35
thought as a, 62
vasculo-postural, 121
Reflexes, action of drugs in relation to, 44
and movements of eye, 72-82
ankle clonus, 39
Babinsky's, 38
canalization of, 39
clinical use of, as means of localization, 38
conditioned, 41
causing hunger contractions, 207
in digestion, 220
controlling rigidity of abdominal wall in inflammation, 41
co-ordination of voluntary movement, 44
effect of strychnine on, 63
exaggeration of, 38-41
in neurasthenia, 192
in tetanus, 39
facilitation of, by repetition, 39
formation of, 42
jaw jerk, 39
of eye, 78
of leg, 36
of skin, 36
plantar protective, 38
postural, and co-ordination, 44
reaction of accommodation, 82
Reflexes, recovery, 38
respiratory protective, 181-183
sensory, 46
Refraction, errors of, 75
Refuss test meal, 225
Renal calculus, referred pain in, 25
Renal threshold, for bilirubin, 254
for sugar, 246
Repressions, elucidation of, 64
Respiration, and maintenance of body neutrality, 267, 270
artificial, Schafer method of, 340
Sylvester's method of, 340
effect of exercise on, 298
failure of, 339
carbon dioxide in treatment of, 341
conditions causing, 338, 339
drugs causing, 339
friction of face and ribs in, 341
rhythmical traction of tongue in, 340
under anæsthesia, acapnia causing, 341
in commencing medullary compression, 6, 7
mechanics of, 152
derangements in asthma, 165
rapid, in shock, 126
Respiratory, adaptations of body, general, 176-180
centre, 145, 146
affections of, 153
diminution in activities of, 148
failure of, causes of, 148
in maintenance of body neutrality, 271
mechanism of, 147
response of, to oxygen, 158
sensitivity of, influence of temperature of blood upon, 148
efficiency, 162
curtailment of, without cyanosis or breathlessness, 164
passages, patency of, 163
protective reflexes, 180-183
quotient, 188
reflex, protective, in asthma, 182
in coughing, 181
surface in breathing, 149
tissue, blood as, 159
Rest, and exercise, 293-307
importance of, in acute heart failure, 142
necessity for, 302
Restlessness in shock, 126
Reticulo-endothelial system, and bilirubin formation, 253
in protection against disease, 311
Retina, 76
detachment of, 76
ophthalmoscopic appearances of, 76
simple hyperanæmia of, 76

Retinitis, pale areas in, 76
Rhinitis, obstruction of Eustachian tube in, 84
Rickets, vitamins A and D in relation to, 197
Rinné's test in middle ear deafness, 86
Risus sardonicus, 20
Romberg's sign, 49
Rotation, sense of, function of semicircular canals in, 49
Rovsing's sign, 27
Rubro-spinal tract, 16

Saline injections, intravenous, in shock, 127
Saliva, secretion of, effect of emotions on, 220
Salivary glands, paralysis of, thirst in, 275
Salts in food, requisite amount of, 190
Scarlet fever, circumoral pallor in, 316
Schafer method of artificial respiration, 340
Schick test in diagnosis of diphtheria, 312
Schwaback's test in pathological changes in canals of cochlea, 88
Scleritis, 73
Sclero-keratitis, 73
Sclerosis, postero-lateral, disturbances of sensation in, 32
Sclerotic, conditions of, affecting vision, 73
Scotoma, vision in, 78
Scurvy, causes of, 279
Secretions, internal, influence of, on metabolism, 211
  psychic, 221
Senile deafness, 88
Sensation, 22-34
  analysis of, in central nervous system, 24
  effects on, of interference with pathways of spinal cord, 31
  hyperæsthesia, 33
  index of, 26
  interference with, various forms of, 30
  mental attitude in, 33
  muscle and joint sense, 29
  of tactile discrimination, 29
  pathways of, 28
  sense of pain, 23
  sensory changes in hysteria, 32
  visceral, 26
Sensory nerve endings, paralysis of, effect on sensation, 30
  paths, lesions of, 31
  reflexes, 46
  stimulation in relation to shock, 125
Septicæmia, acute, temperature in, 284
Shock, acapnia in, 125, 128
  central failure causing, 124
  characteristics of, 123
Shock, effect on circulation, 126
  general considerations, 126
  histamine, 124
  peripheral failure in, 123
  production by chemical substance, 124
  secondary wound, treatment of, 338
  sensory stimulation in relation to, 125
  shallow breathing in, 147
  surgical, 123
    acapnia in, 149
    temperature in relation to, 284
  symptoms of, 126
  treatment of, 127
Sight, associations of areas in brain responsible for, 55
  movements and reflexes of the eye, 72-82
  origin of, 72, 76
Sinus arrhythmia, 98
Sixth nerve, lesions of, effects of, 79
Skin, the, 315-319
  as excretory organ, 318
  colour of, factors influencing, 315-317
    in diagnosis, 315
    quality of blood in relation to, 317
  diseases of, causes of, 319
  excretion by, in kidney disease, 318
    of alcohol, 319
    of drugs, 319
    of urea, 319
  flushed, conditions causing, 316
  functions of, 315
  general state of, 317
  grafting, importance of blood grouping in, 130
  heat and cold spots in, variation of, 22
  in protection against disease, 308
  loss of heat through, mechanism of, 285
  normal, factors governing, 317
  pallor, conditions causing, 315
    in cardiac disease, vaso-motor origin of, 122
    in shock, 126
  rash, distribution of, factors influencing, 317
  reflexes, 36
  secretion of sweat in relation to, 318
  sensations in, 22
  thyroid in relation to, 318
  trophic influence of nervous system on, 317
Sleep, deep, extensor reflex present in, 39
  nature of, 302
  necessity for, 302
  value of, 303
Sleeplessness, causes of, 303, 304
Small-pox, fever in relation to, 290
Sneezing, reflex connected with, 181
Sound, conduction and transmission of, 84, 85

Southey's tubes in treatment of œdema, 279
Speech, 53-59
  association mechanisms in, 53
  degree of association in relation to, 54, 55
  effector mechanisms in, 57
  lesions of receptive association areas, results of, 58
  motor area for, in brain, 15
  psychology of, 62
  receptor mechanisms in, 53
Spelling, associations connected with, area in brain responsible for, 56
Sphygmograph, hot wire, 116
Spinal cord, lesions of, hypertonus due to, 39
  pathways of, interference with, effects on sensation, 31
  reflex, 35
    absence of, 36
    influence of higher nervous centres on, 37, 38
    twofold action of, 40
Squint, convergent, 75
  divergent, 75
Stapedius muscle, function of, 86
  lesions of, 21
Starch, digestion of, in stomach, 221
Starvation, conditions causing, 207
Stasis of blood in relation to clothing, 132
Stereognostic sense, impulses governing, 30
Stomach, and brain, antagonism between, 244
  atony of, and ulcer, diagnosis between, 239
  hydrochloric acid of, in relation to ulcer, 240
  hypersecretion of, 237
  movements of, 226
  musculature and tension of, interference with, 239
  pain referred to margin of ribs, 25
  protein digestion in, 221
  starch digestion in, 221
Stools in diagnosis of cause of jaundice, 255
  undigested matter in, 206
Stramonium, action of, 326
Strophanthin in treatment of heart failure, 143
Strychnine, action of, in heart failure, 144
  in reflexes, 39, 40, 63
  poisoning, facial expression in, 20
Subconscious, movements of the, 60
Subcutaneous tissues, gelatinoid degeneration of, and adiposity, diagnosis between, 318
    and œdema, diagnosis between, 318
Substantia propria of cornea, 72
Sugar, uses of by body, 248
Suggestion in psycho-therapy, 69
Sunlight, in relation to feeding, 189
  in relation to vitamin D, 198
Supra-nuclear lesions in hemiplegia, 21
Suprarenal cortex, and thyroid, antagonism between, 205
Suprarenals, in relation to adaptation, 329
  in relation to shock, 284
  in relation to sympathetic activity, 329
Surgical shock, 123, 149, 284
Swallowing and digestion, 218-228
  disorders of, 218
Sweat, cold, causes of, 318
  secretion of, in relation to skin, 318
Sweating and heat regulation, 285
  excessive, danger of, 281
  stimulation of, by drugs, 281
"Swimming of the head." 8
Sylvester's method of artificial respiration, 340
Sympathetic group of nerves, action of, on circulation, 321
    on digestion, 321
  adrenaline on, action of, 324
  functions of, 321
  histamine on, action of, 325
Sympathetic nerve, aneurysm of, 82
    paralysis of, 81, 82
Sympathetic nervous system, influence on integrity of circulation, 120
Sympathetic-parasympathetic balance, action of nicotine on, 327
  diseases affecting, 322
  effect of drugs on, 324
  endocrines in relation to, 328
  maintenance of, 320
  value of, 324
Syncope due to pooling of blood, 7
Syphilis, influence of, on growth, 213
Syringo-myelia, loss of sensation in, 28, 31
Systole, extra, 99
    differentiation from dropped beat of heart-block, 100
Systolic murmurs, 103

Tabes, absence of light reflex in, 80
  absence of spinal reflex in, 36
  degeneration of posterior nerve roots in, 31
  ptosis in, 79
Tachycardia, 94
Tactile discrimination, sensation of, 29
Talma-Morrison operation for ascites, 279
Taste, localization of, 33
Temperature, diurnal variation of in disease, 283

Temperature, in protection against disease, 314
in relation to vitamins, 198
of body, 283-292
clothing in relation to, 287
diurnal variation of, 283
in relation to infection, 287
in relation to reduction of muscle tone, 284
in relation to surgical shock, 284
normal, 283
regulation of, 284
rise of, causes of, 288
variations of, in different regions, 283
subjective sensation of, 288
subnormal, causes of, 292
in shock, 126
Tenesmus in acute dysentery, 240
Tensor tympani muscle, action of, 86
Test meals, Ewald, 225
Refuss, 225
Van den Bergh, 253
Tetanus, exaggeration of reflexes in, 39
facial expression in, 20
Therapeutics, new psychology in relation to, 65
Thinness, insufficient fluid intake causing, 274
Third nerve, lesions of, effects of, 79
Thirst, a protective mechanism of body, 275
after atropine administration, 220
causes of, 275
in relation to chronic alcoholism, 275
in shock, 127
post-operative, causes of, 275
treatment of, 275
Thought-cycle, 68
Thought, habit or associations of, 63
largely a reflex, 62, 63
psychology of, 62
Thrombosis of cavernous sinus, œdema in, 278
inferior cerebellar artery, effect of on swallowing, 219
Thymus, importance of in early life, 334
Thyroid, the, 202-205
and growth, 213
pancreas, antagonism between, 332, 333
suprarenal cortex, antagonism between, 205
catalytic action of, 202
control of metabolism by, 329
in relation to adaptation, 329
in relation to body weight, 331
in relation to iodine, 203
in relation to skin, 318
relationship of with pituitary, 332
Thyroidectomy as cause of pituitary enlargement, 332
Thyroxin, chemical constitution of, 202
Tinnitus, 89
Tissue, capillaries of, permeability of, 278
culture, 216
repair in relation to feeding, 184
Tobacco amblyopia, scotoma of, 78
Tongue, innervation of, 21
Tonometer, use of, 74
Touch, sensation of, 22
Toxæmia, heart efficiency in, 137
Toxic products, elimination of, in regard to consciousness, 11
Transfusion of blood, 129
"Tripod of Life," 342
Tryptophane, 202
Tuberculin inoculation, rise of temperature following, 288
Tuberculosis, diagnosis of, tests for, 312
diurnal variation of temperature in, 283, 292
influence of, on growth, 213
malar flush in, 316
Tympanic cavity, 84
Tympanic membrane, 83, 84
Typhoid, cold bath treatment of, 290
excessive peristalsis in, 229

Ulcer, duodenal, localized irritation in, 239
gastric, as cause of starvation, 207
dietetic treatment of, 242
localized irritation in, 239
medical treatment of, 242
surgical treatment of, 240
"juxta-pyloric," 239
Unconscious mind, the, 67
Unconsciousness, asphyxia causing, 10
compression of carotids and, 6
earlier in cerebral than in cerebellar tumours, 6
loss of blood and, 7
quality of blood in relation to, 9
Under-eating, effects of, 208
Upper motor neurone, lesions of, 13, 14
Uræmia, abnormal acids in blood in, 273
acid phosphate and, 269
breathlessness in, nature of, 159
treatment of, 10
value of reduction of pressure of cerebrospinal fluid in, 11
Urates in gout, 264
Urea, formation of, 262
in urine, 262
Uric acid in urine, 264
Urine, the, 257-266
ammonia in, 263

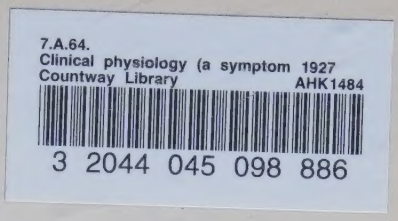
Urine, constituents of, 261
creatinine in, 263
diastase in, 265
examination of, in disease, importance of, 257
excretion of, dyes in, 265
gravel in, relation to fluid intake, 274
hydrogen ion concentration of, 261
oxalates in, 265
phosphates in, 264
quantity and specific gravity of, 258
reaction of, 260
factors influencing, 261
retention of chlorides in, in pneumonia, 281
secretion of, by kidney, opinions on, 257
pituitary body in relation to, 259
urea in, 262
uric acid in, 264

Vaccine therapy, failure in, cause of, 312
Vaccines, autogenous, 311
Vagus, action of, 321
protective function of, 323
tone, influence on rate of heart, 91, 92
Van den Bergh test, 253
Varicose ulcers, treatment of, 317
Variety, necessity of, 305
Vascular tone, reflex nature of, 7
Vasculo-postural reflex, 121
Vaso-motor centre in medulla, influence on integrity of circulation, 120
origin of pallor in cardiac disease, 122
Vegetables, beneficial effects of, 189
Venesection in cardiac œdema, 282
Venous blood, circulation of, factors influencing, 277
Venous distension in acute heart failure, 141
Venous obstruction, anoxæmia due to, effect on capillaries, 172
Venous pressure, 118
an index of cardiac efficiency, 276
influence on rate of heart, 92
Venous pulse, 107-110
Vertigo, due to labyrinthine disease, 50
true, 8
Vestibular apparatus, in relation to equilibrium, 49
Vestibular function, Bárány's eye tests for, 50
Vestibular nerve, lesions of, effects of, 89
Vestibule of ear, disturbances of, 89
Visceral pain caused by stretching, 27
Vision, disturbance of, variations of, 77
field of, mapping of, 78
impairment of, causes of, 73
paths of impulses of, course of, 78
Vital capacity, 154
Vitamins, 197-201
A, deficiency of, evidence of, 198
distribution, 197
A and D, in relation to rickets, 197
therapy, 199
and growth, 213
B, distribution of, 200
B and C, distribution of, 200
C, 200
deficiency of, evidence of, 201
classes of, 197
content of food, 188
D, distribution of, 197
sunlight in relation to, 198
deficiency, and permeability of capillaries, 278
effect of cooking on, 198
effect of pasteurization on, 198, 201
source of, 197
Vitreous humour, 74
Voluntary movement, 12-21
bones and joints in relation to, 18
hysterical paralysis and, 18
pain in relation to, 23
Voluntary muscle, movements of, 16
Vomiting in gastric irritation, 239

Wassermann test, bases of, 311
Wasting diseases, facial expression in, 20
Water, content of body, 274-282
hammer pulse, 102
in food, requisite amount of, 190
"Water intoxication," 281
Weber's test in middle ear deafness, 86
White blood corpuscle, development of, 136
histology of, 134
number of, variation in, factors influencing, 135
Widal reaction, 313
Word blindness, 58
Word deafness, 58
Writing, associations connected with area in brain responsible for, 56

X-ray, diagnosis of intestinal stasis by, 234
for demonstrating peristaltic waves, 227
treatment of hyperthyroidism, value of, 204

TUFTS COLLEGE MEDICAL & DENTAL SCHOOL
DEPT. OF ANATOMY



7.A.64.
Clinical physiology (a symptom 1927
Countway Library AHK1484
3 2044 045 098 886